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THE DIAGNOSIS AND TREATMENT OF INTRATHORACIC NEW GROWTHS

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WITH A CHAPTER ON

RADIOTHERAPY

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Profe o of Rad o he ap Un ve y of Lond n

D e o of he Rad o he apy D pa men Ro a Can e Ho p al

AND A CHAPTER ON

OPERATIVE TREATMENT

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PREFACE

Now that the surgery of the thorax has finally emerged from the experimental stage and has become a recognized speciality in which increasing numbers of consultants are being regularly trained, it has seemed to me worth while to make an attempt to compile a short monograph on new growths of the chest which might be of use, not only to those who will have to deal directly with the radical treatment of these conditions, but also to those general physicians who, encountering them with frequency in their practice, are seeking for reliable information in regard to our present methods of coping with this problem

When I first began the actual writing of this work, the classification of the various tumours and the general arrangement of the chapters presented some difficulty After discussion with the two colleagues who have honoured me by contributing each a chapter on the most important practical aspects of the subject, I realized that a choice had to be made between two main alternatives One of these was to deal with the matter primarily from the standpoint of the operative surgeon, and to divide intrathoracic neoplasms according to their anatomical position, that is to say according as they were in connexion with the bronchi, intrapulmonary, or mediastinal From the operator's point of view this had obvious advantages, but for the general reader it left much to be desired Since the book was not intended primarily as a surgical volume, but rather as a general work, written by a physician, and addressed to all in the profession who were directly or indirectly concerned with lung cancer and other growths in the chest, it seemed better to adopt the other alternative This was to deal with the growths mainly on the basis of their pathological classification, since this would afford a wider appeal to numerous medical men who are genuinely concerned with the subject It is to be hoped that this decision will commend itself to readers Every course of action has its advantages and its disadvantages, one cannot have one without the other I am fully conscious of the many faults and shortcomings of this work, for which I can but crave the indulgence of those of my professional brethren who may choose to pay me the compliment of reading it

I am greatly indebted to many of my friends without whose generous help I could not have undertaken this task To my two colleagues Professor Smithers and Mr Tubbs I offer my sincere thanks, both for their invaluable contributions to the text, and for their forbearance with me in the numerous worries to which I must surely have subjected them Mr Tubbs and I are greatly obliged to our colleague Dr Robert Machray for contributing an important section on anaesthesia in thoracic surgery I have been fortunate in

securing numerous excellent illustrations from various sources other than my own cases, and I should like especially to thank my colleagues from Brompton, Mr R C Brock, Dr Clifford Hoyle, and Dr Simon Dr Campbell Golding has allowed me to choose for reproduction several important radiograms from his radiological museum in the Royal Cancer Hospital, and Professor R A Willis has supplied me with illustrations of tumours from the Pathological Department To both of these good friends I am extremely grateful I have made numerous acknowledgements in the text, for any inadvertent omissions I can only ask the forgiveness of those concerned

As always, I am indebted to my old friend Mr G T Hollis, M A , of the Oxford University Press, without whose hopeful encouragement I might not have ventured on this difficult undertaking

MAURICE DAVIDSON

Harley Street, W 1
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I
INTRODUCTORY

THE problem of the diagnosis and treatment of thoracic neoplasms has lately come more and more into the purview alike of physicians, surgeons, and general practitioners It calls for increasing organization and team-work on the part of those within whose special departments the management of these diseases is now becoming centralized In attempting to deal, more or less comprehensively, with this important subject I must by way of introduction give the reader an outline of the general direction in which our knowledge of this branch of medicine has tended to expand in the last few years

The development of thoracic surgery may be said to have received its main *impetus* from the considerable increase of knowledge acquired during the course of the First World War The information gained in this period was consolidated during the succeeding years and considerable progress was made, especially in connexion with such inflammatory conditions as tuberculosis, bronchiectasis, and lung abscess A further stimulus was supplied a few years later by the increasing interest aroused in the subject of intrathoracic new growths and especially by the apparent rise in the incidence of primary bronchial carcinoma The latter condition, hitherto looked upon as a rarity of academic rather than practical importance, began to assume alarming proportions in the records of chest hospitals and also even in many of the large general hospitals The need for further investigation, by all available methods, became increasingly obvious, and the necessity for more frequent recourse to exploratory thoracotomy, even in cases which held little or no prospect of cure, was recognized as an indispensable preliminary to any real advance in our knowledge It was felt that unless the possibilities of surgery in these cases of malignant disease were fully exploited no progress in treatment could be expected, and in this spirit there began a vast amount of pioneer work in operative surgery which laid the foundation of much of the success that has been recorded in the last decade Not long after the close of the First World War thoracic surgery had achieved a remarkable degree of technical improvement, and exploration of the chest was viewed with no greater apprehension than exploration of the abdomen Today it may be said without contradiction that lung resection, in suitable cases under modern surgical conditions and in expert hands, carries no greater risks than those incidental to any major abdominal operation

One of the most important factors which have contributed to this advance has been the use by the anaesthetist of 'assisted' or 'controlled' respiration

this has done much to lessen the difficulties and dangers encountered in the earlier days of major chest operations Further increases in our knowledge, both in the field of experimental surgery and in that of the physiology and mechanics of respiration, have added to the confidence with which it is now possible to recommend the operative treatment of conditions which formerly [illegible] outside the range of practical surgery, or were at any rate [illegible] greater hesitancy The outlines of such development were [illegible] critical review of the progress of chest surgery published in 1938 by the late Tudor Edwards Since then there has been still further advance in the clinical side of this work

Radiology and radiotherapy have also made considerable strides On the diagnostic side the introduction of sectional radiography has been of much value The method of angio cardiography, though mainly applicable to the surgery of the heart, has also been used and has proved valuable in the recognition of such tumours of the chest as haemangiomata The use of the diagnostic pneumothorax is still valuable in some cases for determining anatomical relations of importance to the surgeon in planning his operative approach

Bronchoscopy has more and more been adopted as an integral part of the routine investigation of patients suspected of having thoracic new growths and has in many cases become a substitute for bronchography, on which not so many years ago the diagnostician placed so much reliance

In the field of X-ray treatment a marked improvement has been achieved in technique, based on research by the physicists and on the increasing clinical experience of the radiotherapists Not only has the value of deep X-ray therapy been enhanced as a palliative, but it has established a claim to be considered more seriously as a possible means of effecting a cure, alone or in combination with surgery, of some patients with malignant disease within the chest

The demonstration of malignant cells in the sputum by an extension of the wet-film method for examination of tumours and fresh tissues was described in 1935 by Dudgeon and Wrigley In their series of 58 cases particles of new growth were found in 26 The diagnosis was confirmed in 8 of these by bronchoscopic examination, and in 11 by biopsy or autopsy in the remaining 7 no further confirmation had been received up to the time of the publication of their paper A further investigation was recorded some years later by Sambrook Gowar, who examined the sputum from 93 cases of suspected pulmonary new growth and demonstrated malignant cells in 64 3 per cent of proved or probable instances of carcinoma In Russia Althayzen has reported 70 per cent , and Wandall in Denmark 86 per cent of positive diagnoses Herbut and Clerf in a general review record 22 positive diagnoses

in a series of 30 consecutive cases (73 per cent), but state that corroboration by microscopic examination of biopsy specimens in the same series was only obtained in 11 cases (36 per cent)

The accurate identification of tumour cells in sputum by this method

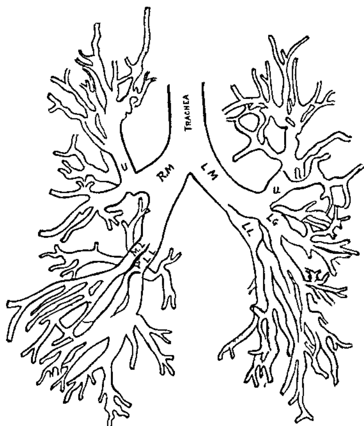


FIG 1 Diagram of the bronchial tree (antero-posterior view) *R M* right main bronchus *L M* left main bronchus *M L* middle lobe bronchus *U* upper lobe bronchus *LG* lingula *L L* lower lobe bronchus

demands constant practice and considerable histological experience It is not, of course suggested that this test should replace other methods of examination, but it has proved in expert hands to be of undoubted value in helping to establish the diagnosis in some cases in which other methods have failed and also in some very ill patients whose condition was such that they could not be subjected to bronchoscopy It has equally led to errors of diagnosis in the hands of the inexpert

In cases in which operation is definitely not contemplated the diagnosis may often be confirmed by removal of a piece of tumour by aspiration for biopsy, especially when the tumour involves the chest wall

I have spoken of bronchoscopy as a part of the routine in the investigation of thoracic neoplasms prior to treatment In connexion with this I would

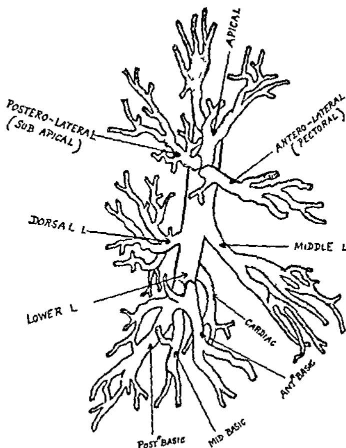


Fig 2 Diagram of the bronchial tree (right lateral view)

call attention at this point to the importance now attached to the anatomy of the bronchial tree and its relation to the various pulmonary areas The conception of a broncho pulmonary segment, that is of a particular branch of the bronchial tree with the corresponding area of the lung parenchyma aerated through it, is not new It was described by some anatomists in the latter part of the nineteenth century, but little or no attempt was made to recognize its bearing upon practical problems of medicine and surgery until a comparatively recent date The latest developments of radiology and

bronchoscopy have compelled a revision of the traditional descriptions of the anatomy of the lungs and bronchi, and the work of Nelson, Foster-Carter, Brock, and many others has brought into prominence the practical application of the now accepted conception of the broncho-pulmonary segment

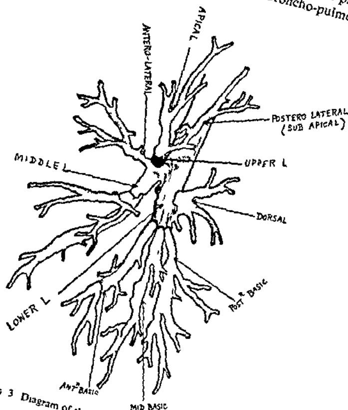
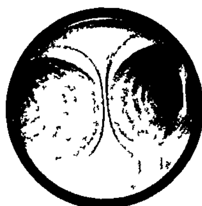


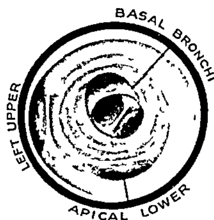
Fig 3 Diagram of the bronchial tree (left lateral view)

This has been defined by Foster-Carter and Hoyle as 'the portion of lung served by a principal branch of a lobar bronchus' such a branch being termed 'a segmental bronchus' Attempts have been made to arrive at some conformity in the nomenclature of the bronchial divisions, and while there is as yet no universal standard table, the following may be taken as representing that which is generally accepted and which is here illustrated for the reader's convenience by the semi diagrammatic representations of the bronchial tree shown in Figs 1, 2 and 3









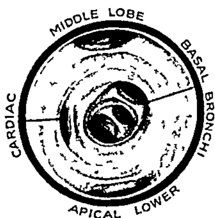


FIG 4 Bronchoscopic appearances at different levels (By courtesy of R C Brock F R C S)

TABLE I *Nomenclature of Bronchial Tree*

R ght	*Left*
Upper lobe bronch s	*Upper lobe bronchus*
1 Antero lateral (pectoral)	1 *Ascend ng branches*
2 Ap cal (ascend ng)	Antero-lateral (pectoral)
3 Postero lateral (sub ap cal)	Ap co-posterior
	ap cal
M ddle lobe bro chus	postero lateral (sub-ap cal)
1 Anter or (med al)	2 *M ddle branches* (Lingula)
2 Lateral	*lateral (ax llary)*
	Anter or
Lower lobe b onch s	
1 Dorsal	*Lower lobe bronchus*
2 Card ac	1 Dorsal
3 Anterior bas c	2 Anter or bas c
4 M ddle bas c	3 M ddle bas c
5 Poster or bas c	4 Posterior basic

D stribut on of the ma n branches of the r ght and left bronchi (see also F gs 1 2 and 3)

TABLE I A *Proposed International Nomenclature of the Bronchial Tree compared with various other schemes*
[From the report by the Thoracic Society (loc cit)]

In na onal nom nclo ure	*Brock*	*Ja kson and Hube*	*Hu .inga*	*Kou ky e al*	*Fo er-Ca e*
RIGHT					
Uppe lobe bronchus					
Apical (1)	Pecto a	An erior	Pectoral	Anterio } La eral	An ero a e al
Poste or (2)	Sub-ap cal	Pos erior	A ary	Po e io } La eral	Pos ero-late a
An e o (3)	Ap cal	Apical	Ap ca	Ap cal	Apical
Lowe part of igh main b on hus	—	—	—	—	Descend ng
Midd e lobe bron hu					
La e al (4	La e a	Lateral	Late al	La e a	Lateral
Med a (5)	Med al	Med a	Med al	An e or	An e ior
Lower lobe b on hu					
Apical (6	Ap cal	S pe o	Uppe dorsal	Apical	Dorsal
Med al ba al (ca d ac) (7)	Ca d ac	Med a basal	Ca d al	Med al	Card ac
An e o ba al 8)	An e o ba al	An e o basal	Uppe ven ra	An erio	An e o ba c
Late al basa (9	M dd e basa	La e a basal	Lowe en a	La e al	M dd e ba c
Po e o ba al 0)	Po e or basa	Pos e o basal	Lowe dorsa	Po e o	Pos erior bas c
LEFT					
Uppe lobe bronchus					
Uppe d on	Ap co-pec o al	Uppe d on	—	—	Ascend ng
Ap cal (1)	Ap ca	Ap ca	Apical	Apical	Apical
Ap co-pos e or (1) and (2	—	Apical pos e o	M dd e	—	Apico pos e o
Pos e o (2	Sub-apical	Pos e o		Pos erio	Poste o-la eral
An e io (3	Pectora	Ante io		An erio	An ero-la e a
Lingu a (we d ision)	L ngu a	Lowe (ngula) *di ision*	An erior	L ngula	L ngula
Supe io (4	Upper	Supe o		Uppe	Lateral
In erio (5)	Lowe	Inferio	—	Lowe	An e ior
Lower lobe b on hu					
Apical (6)	Apical	Superio	Dorsal	Apical	Dorsal
An e ior basal (8)	An e or basal	An erio -medial basal	Late al ven ral	*Ante ior*	*Anterior ba ic*
La era basa (9)	Middle basal	La eral basal	} Dorsal medial	La eral	Middle basic
Poste ior basal (10)	Pos e ior basa	Posterior basal	} Dorsal medial	Posterior	Poste ior basic

Since Table I was sent to press, the Thoracic Society has published its observations on the need for uniformity in the nomenclature of broncho-pulmonary anatomy For the sake of completeness I have reproduced the results of the deliberations of the sub committee, already published in tabular form (*vide* Table I A)

The appearances of the different portions of the bronchial tree accessible to the bronchoscope are shown in the accompanying illustration (Fig 4)

Correlation of the bronchoscopic findings with the X-ray appearances (e g of opacities indicative of segmental pulmonary collapse due to obstruction by growth of the corresponding bronchus), is part of the routine investigation in cases of suspected intrathoracic neoplasm, and may give information of significance in regard to the localization of the lesion Even if a bronchial tumour cannot be seen through the bronchoscope owing to its being in a situation outside the line of possible vision, the surgeon may yet acquire important information from visible distortion of some part of the bronchial tree (e g the main carina, or occasionally one of the lesser carinae between subdivisions of a bronchus) which not only affords confirmatory evidence in suspected cases but may also determine the likelihood or otherwise of operability and the decision whether or not an exploratory thoracotomy should be undertaken This will be discussed in greater detail later on (see Chap XIV, Operative Procedure)

In the foregoing paragraphs I have endeavoured briefly to outline the present position of medicine, surgery, and radiology in relation to thoracic new growths, and to indicate the main lines along which our knowledge of these conditions has gradually developed In the succeeding chapters I shall give an account of the various groups into which I have thought it convenient to divide these lesions, and shall endeavour to give a composite picture of the condition in each of these as it presents itself to the clinician in practice Diagnosis of any individual tumour, though more evident in some cases than in others, is often a matter of real difficulty and nearly always involves a considerable amount of team work and the piecing together of numerous links in the whole chain of evidence The most experienced radiologists are only too well aware of the difficulties of interpreting the significance of shadows cast by tumours in the chest, and, so far from being able from the radiological appearances alone to identify the nature of a circumscribed opacity, are sometimes in doubt as to whether the lesion is inflammatory or neoplastic I have already indicated that bronchoscopy, though almost always regarded by the surgeon as a *sine qua non* without which he would be unwilling to proceed to thoracotomy, may sometimes fail to give any positive information Moreover, even exploration of the chest on the operating table

is not necessarily an infallible guide to diagnosis for example in the case of an intrapulmonary mass situated deep within a lobe In such circumstances if thoracotomy is proposed it is sometimes necessary to plan beforehand for a lobectomy or a pneumonectomy and to face the possibility of removing a lobe or even a whole lung for what may eventually prove to be an inflam matory lesion since it is disastrous to leave untouched an operable carcinoma There is some consolation in the fact that inflammatory lesions resected under the false diagnosis of tumour (for example tuberculomata) would probably have required such treatment in any case However with proper care in investigation errors in diagnosis such as this should be reduced to a minimum

I have dwelt upon the above considerations mainly because of the bearing they have on the problem as it presents itself alike to the general practitioner, who looks to the specialist for guidance and to the unfortunate patient The latter is usually in no position to judge of the matter and is wont *in the great* majority of cases to rely on his regular medical adviser for an interpretation of the observations of those experts who have been called in as a final court of appeal The conclusions of the latter are not infrequently expressed in a fashion so detached and impersonal as to constitute something of a mystery not merely to the patient but possibly even to the patient s own doctor Apart altogether from the purely technical difficulties which often surround the conduct of such cases there still remains the duty of so handling the matter as to give an explanation to the patient and or his relatives such as will enable them to grasp the essentials of the situation and to realize its implica tions In accepting the final decision of experts a certain responsibility lies upon the shoulders of the lay public concerned from the onus of which their ignorance of the technical aspects of the matter cannot wholly relieve them

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II

ADENOMATA

BENIGN AND MALIGNANT GROWTHS

BEFORE discussing in detail the various thoracic neoplasms to be described in the following chapters, it is, perhaps, necessary briefly to consider what is meant by innocency and malignancy as applied to tumours It must be remembered that the expressions 'benign' and 'malignant' are really arbitrary terms which have been commonly adopted as a convenient practical indication of the general behaviour of a new growth and of its effects, immediate and remote, upon the human body Many tumours which are ordinarily classified without dispute as benign may ultimately cause the death of the patient because, having attained a considerable size, they encroach upon vital structures and by pressure upon various organs render their normal functions impossible Though innocent in the accepted pathological sense of the word, such tumours kill eventually by their purely mechanical effects It is also true that there are tumours which, though by reason of their mode of spread in the tissues and their dissemination to parts of the body remote from the original site of growth they are rightly designated malignant, yet grow and spread so slowly that their ultimate effects are long delayed, in these circumstances death of the individual may take place from some other disease process that has no direct connexion with the tumour Moreover, it is recognized by pathologists that there are varying degrees of malignancy in tumours which resemble each other in the general type of their cellular structure, and also that growths which have for long periods manifested features that are ordinarily regarded as innocent may ultimately take on characteristics that are properly associated with malignancy Although in the main a broad division can be made between innocent and malignant tumours, based on histological structure, mode of growth, and behaviour in respect of metastatic spread, there are instances in which a hard and fast distinction cannot be maintained, and the pathologist may find himself unable to give a categorical diagnosis, and may be compelled to report in somewhat general terms on the character of the material supplied to him

Broadly speaking, it may be said that the benign growths tend to preserve an anatomical structure resembling that of the tissue in which they have their origin, that they are usually more or less circumscribed, with a tendency to encapsulation, that their growth is relatively slow, and that they do not spread to remote parts of the body by metastasis Malignant growths on the other hand are frequently less differentiated in structure, more rapid in their

growth, and likely to give rise to widespread deposits of their component cells via the blood-vessels or lymphatics So far as any one of these features alone can be said to be distinctive, it is this phenomenon of metastasis which is commonly regarded as generally characteristic of malignancy and which forms the chief criterion on which the arbitrary division of tumours into innocent and malignant is usually based

It is in the light of these general considerations, to which I would particularly invite my readers' attention, that I propose to deal with the practical problems of diagnosis and treatment of the various forms of neoplasm that are found in association with the chest

ADENOMATA

Adenoma of the bronchus is now generally recognized as by far the commonest of the benign growths in this region Up to a comparatively recent date these tumours were frequently regarded as malignant, and credit was taken for the successful removal of neoplasms which were alleged at the time to be primary bronchial carcinomata but which subsequent revision of their histological characters showed to be examples of adenomata Adenomata (Figs 5–9) are epithelial tumours, of glandular origin, consisting of masses of cells having a regular tubular or acinar arrangement, consisting of together by a connective tissue which is commonly very vascular and held are usually cuboidal, though columnar or flattened cells may be found in the walls of the alveoli The supporting stroma varies in amount, being sometimes relatively scanty, at other times in excess (fibro-adenomata) A limiting basement membrane can often be made out, and the tumour within the bronchus is often covered by an epithelial layer, consisting of ciliated columnar cells and continuous with the normal lining of the bronchus itself

Such are the typical histological features of the bronchial adenoma, but this characteristic glandular arrangement of the tumour is by no means invariable According to Foster Carter, who has given one of the best general accounts of the subject, about two-thirds of these growths show a much less highly differentiated structure, the appearances in many cases resembling those of the adeno carcinomata from which at first it may be difficult to distinguish them In his review (1941) he recognizes two main histological varieties one exhibiting the definite tubular or alveolar arrangement just described, the other having a less typical glandular structure and an irregular cell content which may at first render it difficult to distinguish the growth from a small celled carcinoma Many of the earlier recorded cases of adenoma were in fact diagnosed as undifferentiated carcinomata

It would seem that in any individual tumour there is little variation in the size and shape of the cells, which are generally all of the same type, having

more or less uniform staining reactions Mitotic figures are rare, and cellular invasion of the stroma is not apparent as it is in the malignant growths, nor is there evidence of excursion of the cells into the blood-vessels or lymphatics MacDonald in a review of 44 cases at the Mayo Clinic refers to the possible confusion between bronchial adenomata and small celled bronchogenic car-



FIG 5 Macroscopic appearances in bronchial *adenoma the middle lobe bronchus is completely* occluded by the growth which was shown on microscopic section to be a benign adenoma (cf Fig 8) (Photograph of specimen in the Brompton Hospital Museum)

cinomata The two main points of distinction which he emphasizes are the absence in the tumour cells of mitotic figures, and the non-occurrence of degenerative processes (pyknosis, karyorrhexis, and necrosis), features which often characterize the malignant growths but which are usually lacking in the case of the adenomata The fact that they do invade the bronchial wall has been responsible for the suggestion that adenomata may be regarded as having a certain local malignancy Their inclusion among the benign tumours is based on the absence for the most part of evidence of metastasis It has been almost universally stated that metastatic spread is unknown, but Adams and his colleagues (quoted by Willis) have recorded it in the case of some



Fig 6 Macroscopic appearances in bronchial adenoma showing a pedunculated intrabronchial tumour there is some bronchiectatic dilatation in the posterior basic segment (Photograph of specimen in the Brompton Hospital Museum)



Fig 7 Macroscopic appearances in bronchial adenoma the main lower lobe bronchus is completely occluded by a growth which extends down the lumen for about two inches microscopic section showed a typical adenoma (cf Fig 9) (Photograph of specimen in the Brompton Hospital Museum)

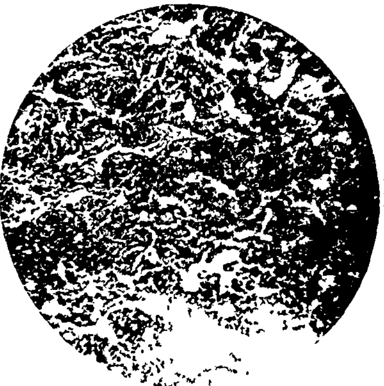


FIG 8 Microscopic appearances in bronchial adenoma (Microphotograph of specimen shown in Fig 5)



FIG 9 Microscopic appearances in bronchial adenoma (Microphotograph of specimen shown in Fig 7)

tumours which appeared to be of this type, and Willis himself describes an example from his own observation of multiple metastatic growths in a young woman who had had repeated haemorrhages from a primary intratracheal tumour, the glandular structure of which resembled that of the adenomata In common with other observers he regards this group of tumours as rightly included among the benign neoplasms, as ordinarily understood, but adds the warning that an occasional exception, similar to that of his own recorded case, must always be envisaged as a possibility In only 1 of the 44 cases from the Mayo Clinic was invasion of a lymphatic gland found, and this MacDonald seems to have regarded as in all probability an example of direct invasion by the primary growth rather than of metastasis

Macroscopically, adenomata appear as endobronchial tumours arising from the bronchial wall and projecting into the lumen the covering epithelial layer, derived from the normal bronchial mucosa with which it is in fact continuous, is usually unbroken The growths may be sessile or polypoid They tend to infiltrate the wall of the bronchus and may penetrate it and extend outwards into the lung tissue, forming a dumb bell tumour, as in the case of some of the neuro-fibromata (cf Chap IV) In some instances the extra-bronchial portion may attain a considerable size, and may appear radiologically as an intrapulmonary growth, though actually the lung tissue has not been invaded, but merely pushed aside (*vide* Fig 7) All observers have noted that these growths occur only in the large bronchi (either the main stem or one of the primary divisions), never in the smaller peripheral branches, as may be the case with some of the carcinomata These anatomical and histological features are illustrated in the accompanying Figs 5–9

Fig 5 shows a specimen from a woman aged 34 who first complained of pain in the right side of the chest a few months later she had a slight febrile attack from which she recovered without special treatment Five months after this she was examined in a mass radiography survey, when an abnormal shadow was seen in the radiogram Bronchoscopic examination revealed a tumour blocking the right middle lobe bronchus Subsequent a right pneumonectomy was performed The specimen shows a shrunken and collapsed middle lobe The middle lobe bronchus is completely occluded by a large tumour, the extrabronchial portion of which is spherical and about 4 5 cm in diameter It is well encapsulated The microscopic sections of both extra- and intrabronchial portions of this tumour illustrate a typical benign adenoma (Fig 8)

Fig 6 shows a specimen from a man aged 50 who came to hospital on account of recurrent attacks of haemoptysis A left lower lobectomy was performed from which the patient made a good recovery This specimen shows a white pedunculated intrabronchial tumour There is some bronchiectatic

dilatation in the posterior basic segment Histologically this tumour was found to be a typical bronchial adenoma

Fig 7 shows a specimen from a man who had been in apparent good health but who was found in a mass radiography survey to exhibit radiological appearances suggestive of obstruction of the right lower lobe bronchus A diagnosis of bronchial adenoma was made, but nothing further transpired until 2½ years later when he had a slight haemoptysis A little later he was examined with the bronchoscope and a firm vascular tumour was seen in the antero lateral segment of the right lower lobe A right lower lobectomy was performed, the patient making a good recovery The specimen shows the main lower lobe bronchus completely occluded by a tumour which has extended down the lumen for a distance of about two inches

The microscopic section of this tumour (Fig 9) shows a typical adenoma The cells are arranged in acini and are very irregular No mitotic figures were seen, nor any evidence of cell division

Incidence, &c. I have said that the adenomata are now generally regarded as the commonest among the different varieties of benign intrathoracic growths For advance in our knowledge of the subject we are largely indebted to the account published in 1932 by Wessler and Rabin of 17 cases of benign intrabronchial tumours, 14 of which these authors observed clinically and identified by examination of biopsy specimens obtained through the broncho scope Since then numerous contributions to the literature have appeared, of these Foster-Carter's is probably the most comprehensive account, from which it appears that in a series of 453 cases of bronchial neoplasms there were 22 examples (i e 4 8 per cent) In this review the average age at the onset of symptoms was found to be 28, the majority being recognized between the ages of 30 and 40 There is little difference between the sexes In the Brompton Hospital series of 22, 12 occurred in men and 10 in women, and of the total cases recorded 62 per cent occurred in women Nothing is known of the aetiology of this type of growth

Clinical and Radiological Features. Like other benign tumours, adenomata may grow to a considerable size before they are discovered When small they may cause no symptoms at all, but owing to their vascularity they are liable to give rise to haemorrhage, and in an appreciable proportion of cases the patient seeks advice in the first place on account of haemoptysis This is usually the main symptom (81 per cent of the Brompton series) Though generally small in amount, the haemorrhage is often recurrent, occasionally a profuse haemoptysis may occur Apart from haemorrhage, the symptoms which present are those associated with the effects of bronchial obstruction with the concomitant changes in the pulmonary segments distal to such obstruction Cough, wheezing, and shortness of breath are common, and if the

factor of infection is added to the mechanical effects of lung collapse the patient may exhibit varying degrees of toxaemia A history of recurrent febrile attacks from this cause is not uncommon

Physical signs alone will seldom if ever decide the cause of the condition, which is brought to light by radiological examination and bronchoscopy An

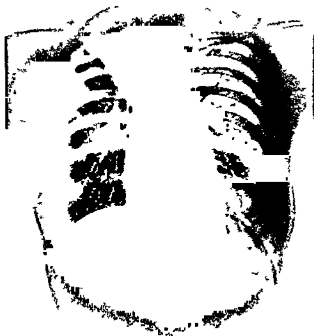


Fig 10 Radiogram from a case of vascular adenoma of the right upper lobe bronchus with collapse of the corresponding pulmonary segment (By courtesy of Dr Campbell Golding)

ordinary tele-radiogram may show pulmonary collapse, segmental or lobar, and bronchography may give evidence of bronchiectatic dilation within the collapsed portion of lung (*vide* Figs 10 and 11) The diagnosis in practically every case is finally determined by bronchoscopy, which may reveal a smooth, pinkish white tumour, for the histological character of which it is necessary to examine a biopsy specimen

Differential Diagnosis. From what has just been said of the clinical and radiological aspects of these cases it will be realized that the diagnosis of

bronchial adenoma is by no means always an easy matter In some cases in which the patient seeks advice on account of haemoptysis the most careful physical examination of the chest may show nothing abnormal, and the physician may be not a little disconcerted to find a similar absence of pathological features, not only in the straight X-ray film, but also in the bronchogram This may well be the case if the tumour is of small size and situated in



Fig 11 Bronchogram from the same case as Fig 10 showing bronchiectatic dilatation within the collapsed right upper lobe (By courtesy of Dr Campbell Golding)

one of the primary divisions rather than in a main stem bronchus In such circumstances the tumour which has failed to show a radiological abnormality may yet be detected by a careful bronchoscopic survey

The causation of haemoptysis in a young adult in whom tuberculosis and morbus cordis have been definitely excluded is occasionally a difficult problem, and the possibility that the haemorrhage may be due to a bronchial adenoma should not be forgotten In the case of patients who present themselves with a clinico radiological picture of bronchiectasis, it must be remembered that the condition may be secondary to partial bronchial obstruction and that an endobronchial tumour may be acting as a foreign body Not a few cases have been subjected to long periods of symptomatic treatment for bronchiectasis as though the latter were a disease *sui generis*, before the real cause of the trouble has been discovered in the shape of an adenoma

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III

DERMOIDS AND TERATOMATA

DERMOID cysts and teratomata, though differing to a varying extent in pathological structure, are usually, for practical purposes, classed together in the literature of thoracic surgery When these tumours are found within the chest the problem which presents itself is mainly one of the danger, either actual or potential, of development of pressure effects which will ultimately kill the patient The possibility of malignant change in some of these growths has also to be taken into account In the earlier stages of growth, when the tumour is small in size, operative removal may be comparatively easy, and since there is no question of widespread metastasis as in the case of the carcinomata and sarcomata, intrathoracic dermoids and teratomata have been included among the benign as distinct from the malignant growths of the chest as ordinarily understood Much has been written about their aetiology, but even now there is no absolute consensus of opinion on this subject, though recent pathological research has done much to clarify the uncertainty which has for a long time been felt as to their origin

Ewing, in his classical work, has described the dermoids as falling into two main groups according to their structural characteristics, (1) the simple dermoids and (2) the teratoid tumours The former he regards as single or multilocular cysts which have a smooth or occasionally polypoid epidermal lining in which are found dermal glands Hair and sebaceous material are the commonest constituents of the contents of the cyst, but in some cases the presence of bone and cartilage has been reported and even portions of thymus gland Teratoid tumours, on the other hand, are more complex in structure and are described as tridermal, since in addition to epidermis, they may contain bone, cartilage, nervous tissue, intestinal tract, respiratory ciliated epithelium and occasionally thyroid, in other words, they appear to originate from all the three divisions of the primordial germ layer Willis after considerable and detailed study of the pathology of these neoplasms, inclines more and *more to regard the dermoids and the teratomata as having* a common aetiology and deprecates the attempt to separate them, as was formerly done, by any hard and fast line of distinction He defines a teratoma as 'a true tumour or neoplasm composed of multiple tissues *of kinds foreign to the part in which it arises*' (my italics) He points out that the more careful and exact the examination of these growths the more apparent it becomes that they cannot be regarded as originating from only one primordial germ layer and the greater is the variety of tissues discovered in them He notes that

even in the simplest so-called dermoid cysts, searching examination will usually reveal the presence of tissues of mesodermal and endodermal origin in addition to skin and adipose tissue For these reasons he looks upon all teratomata as tumours of a single class and regards the attempt to segregate them into subdivisions as purely arbitrary, whether such division is based upon alleged structural differences or upon the clinical behaviour of the various tumours, though it is admitted that those composed mainly of mature forms of tissue are generally benign, while those containing embryonic tissues tend to be relatively malignant

Although there is considerable variation in the structure of the growths included in this general class, they may for practical purposes be divided into two main groups, (1) the simple dermoid, and (2) the teratoma of more complicated structure The simple dermoid commonly occurs in the form of a cyst, the wall of which consists of epidermis, derma, and dermal glands The lining epithelium is usually of the stratified squamous type, though transitional variations in the cells are not uncommon, cilia may or may not be present Cysts are usually single and unilocular, but occasionally two or more cavities are found Cholesterin crystals may be present in the fluid within the cyst In the teratomata a greater variety of tissues is discovered The distinction between these and the simplest dermoids is not hard and fast, and, as Willis observes, is somewhat arbitrary Teratomata may be described, roughly speaking, as more solid in character, though on section they may turn out to be partly cystic As I have already pointed out, these growths vary in their potential malignancy According to Lloyd Rusby it would appear that 70 per cent of those which show malignant change have originated in solid teratomata, while only 30 per cent have come from tumours of the simpler dermoids

Incidence. From the general physician's point of view these growths must be reckoned as uncommon, though not among the rarest of the benign tumours of the chest Up to the end of 1932 Hedblom collected 185 cases from the literature, to which he added 6 of his own in a paper on intrathoracic dermoid cysts and teratomata read before the 16th annual meeting of the American Association for Thoracic Surgery at Washington in May 1933 Lloyd Rusby in a more recent communication has traced 245 cases in all in the literature up to the end of 1939

The condition is found mostly in young people In Hedblom's *series* the age-incidence is given below (Table II)

The majority of cases are thus seen to occur in young adults in the middle twenties It would appear that the tumours are originally due to some error of development occurring in the embryonic period of life, and that they remain latent for a considerable time, usually until the period of puberty,

when some environmental factor or factors determine their awakening to growth, though clinical manifestation may still be delayed for a considerable time Sex appears to play little part out of Hedblom's series of 191 cases 79 were males and 92 were females, the sex in the remaining 20 being unrecorded Out of 177 cases reviewed by Rusby 86 were males and 91 females

TABLE II *Age-Incidence of Dermoids* (Hedblom)

Under 12 years	26 cases [*sic*]	under 12 months 6 1 to 5 years 6 6 to 12 years 10
12 to 16	13	
17 to 20	28	
21 to 30	64	
31 to 40	21	
41 to 50	11	
51 to 60	8	
61 to 70	1 case	

Lloyd Rusby's table shows a similar state of affairs

TABLE III *Age Incidence of Dermoids* (Lloyd Rusby)

0 to 9	17 cases
10 to 19	27
20 to 29	68
30 to 39	37
40 to 49	11
50 to 59	13
Over 60	1 case

Location It is a matter of general experience that dermoids are situated in the anterior mediastinum and are not often found posteriorly They may be situated behind the sternum and between the mediastinal pleurae, occasionally they are seen in the suprasternal notch or behind one of the sternoclavicular joints, the majority are in the so called sterno lateral or lateral positions i e in the mediastinum and extending into one or other side of the thoracic cavity or else mainly in one side of the thorax Duval and Clerc, in a series of 176, found 13 retrosternal, 19 cervico retrosternal, and 144 sterno lateral or lateral in position

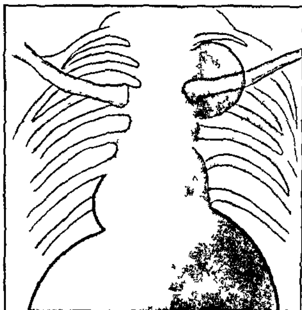
Clinical and Radiological Features As with other tumours within the chest the outward manifestations depend upon the size and position of the mass and the extent to which it has begun to encroach upon other organs and to cause pressure that may give rise to symptoms or to abnormal physical signs In quite an appreciable number of instances the existence of the tumour has been discovered accidentally, either in a mass radiographic survey of a large number of persons or in an individual who has sought medical advice for some independent condition, serious or trivial, and has had an X ray examina tion of the chest as part of a routine investigation Cough and pain in the

chest are the two commonest initial symptoms when once clinical manifestation has begun, difficulty in swallowing and hoarseness may occur with tumours of appreciable size Physical signs, except in cases of very large growths, seldom give information of much practical value Dullness on percussion is usually to be found, with possibly some slight alteration in the character of the respiratory murmur Where there is gross pressure there may be some apparent bulging of the chest wall, and oedema, cyanosis, and enlargement of the superficial veins on the surface of the chest or in the neck have been described In cases in which the condition has been present for *a long time, attention may be called to it by reason of the occurrence of some* complication, such as infection, or rupture of the cyst, either into a bronchus, or into the pleural cavity, the pericardium, the superior vena cava, or even the aorta In some cases recorded the occurrence of a bronchial fistula following rupture of the cyst was shown by the patient's coughing up hair in the sputum In most of the cases with which I have been acquainted, symptoms if present, have not been of a very serious character, and the condition has been brought to light by the radiologist

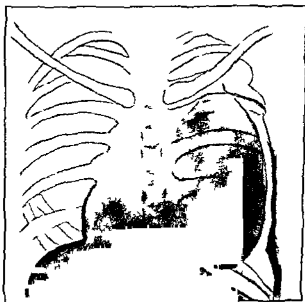
The radiological appearances of these tumours are similar in general to those of other benign neoplasms There is a round or oval shadow with clearly defined edges, situated in the mediastinum, usually in the anterior part, but occasionally posteriorly These features are illustrated in the accompanying diagrams (Figs 12, 13, and 14) which are tracings made from typical radio grams Occasionally the shadow is more irregular in shape as in Fig 15 The anterior position, seen in the lateral view, is the more usual, and is sometimes adduced as presumptive evidence in favour of the diagnosis of a dermoid as against some other variety of tumour this is, however, by no means invariable The position of the shadow in the superior-inferior axis varies According to Shanks and others it generally lies below the level of the aortic arch, but they quote cases published by Liebmann and Chaoul in which the tumour was seen to occupy the superior mediastinum, the aortic knuckle being obscured and the appearances suggesting the presence of an aortic aneurysm or a thyroid tumour or persistent thymus

These points are illustrated for the most part by the following cases

Figs 16, 17, and 18, are from a child of 10 years who was admitted to Brompton for investigation with a history of pain in the left side of the chest which had come on suddenly in the summer of 1930 and had continued off and on ever since Examination of the chest revealed dullness with diminished respiratory murmur in the upper part of the left side both in front and behind The dense opacity seen in the left middle zone was seen in a lateral radiogram to be lying anteriorly behind the second and third interspaces in the mid-clavicular line The density of the opacity was more or less homogeneous, but



F G 12 D agram of rad ogram from a case of a dermo d cyst n the left med ast num (after Lenk)



F G 13 D ag am of rad og am from a case of la ge dermo d cyst n the left med a num (af er Lenk)



FIG 14 Same case as Fig 13 left lateral view (after Lenk)

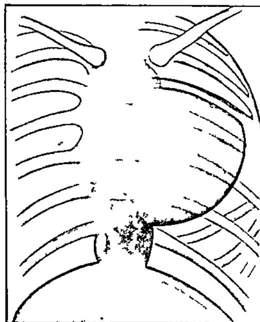


FIG 15 Diagram of radiogram from a case of mediastinal dermoid (From Davidson *Cancer of the Lung* Bristol 1930 John Wright & Sons)

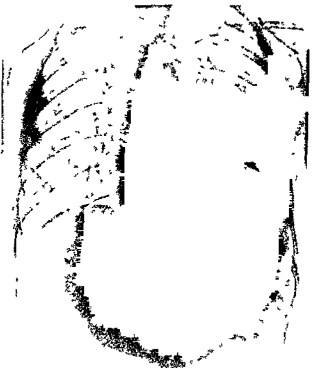


FIG 18 Same case as Fig 16



FIG 19 Specimen of teratoma removed at operation same case as Fig 16 (Drawing of specimen in the Brompton Hospital Museum)

some irregular increase in density was observed in small areas, the appearances were regarded as strongly in favour of a teratoma containing a fragment of bone This proved to be the case when the tumour was successfully removed by operation on September 30th, 1931 The macroscopic appearance of the tumour is seen in Fig 19 Histological examination of a piece of tissue attached to the main mass of growth showed appearances characteristic of thymus gland

Figs 20 and 21 are from a young woman aged 19 who had been complaining of some shortness of breath on exertion she had had a certain amount of cough with occasional substernal pain Examination of the chest revealed a dull area over the upper half on the right side in front and behind, with diminution of the breath sounds The opacity seen in the postero-anterior radiogram is a typical rounded shadow with a sharply defined lower margin The radiologist reporting on the films suggested that the tumour was in all probability a benign growth, but expressed no opinion as to its exact nature It will be seen from the lateral view (Fig 21) that the tumour lies posteriorly, and might for this reason have been diagnosed as a neuro-fibroma rather than as a dermoid Actually this was not the case The growth was removed by operation in two stages, and proved to be a teratoma, a section of the cyst wall showing glands, blood vessels, cartilage, connective tissue, and a lining membrane of columnar epithelium

Figs 22 and 23 show appearances rather different from those of the two preceding cases The postero anterior radiogram displays a large but somewhat ill-defined opacity on the right side from which alone it would seem hardly possible to suggest any positive diagnosis The lateral oblique view (Fig 23) shows the irregular density in the mass and the dark shadows in the upper part of the growth which were thought to be pieces of bone (? teeth) from which the diagnosis of teratoma was made This was verified later, the tumour being removed by operation when it was found to occupy the right anterior mediastinum Pathological examination confirmed that it was a teratoma containing teeth This patient was a young man aged 27 Five years before admission to Brompton he had had slight staining of the sputum for 2 days Otherwise there was nothing of note in the previous medical history In January 1938 he complained of sharp stabbing pain in the lower part of the right axilla, and also of a dry cough On admission he was found to have some impairment of resonance over the right clavicle and in the right supra clavicular fossa also in the first three interspaces anteriorly There was some diminution of the respiratory murmur in this area, no adventitious sounds were heard There was a moderate degree of clubbing of the fingers Thoracotomy was performed on March 16th The operation was a matter of great difficulty, the large tumour being adherent to the pericardium and to other

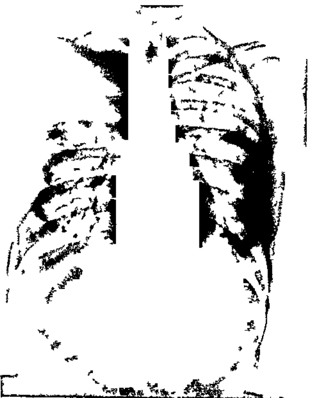


FIG 20 Med ast nal teratoma



FIG 21 Same case as F g 20 r ght lateral v ew



FIG 22 Mediastinal teratoma



FIG 23 Same case as Fig 22 oblique view Showing teeth within the growth

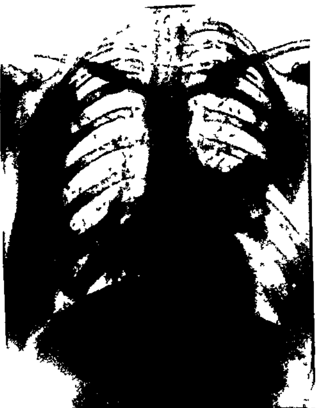


FIG. 24. Calcified dermoid



FIG. 25. Same case as Fig. 24, left lateral view. Showing anterior position of growth

surrounding structures The cyst was evacuated, complete removal being impossible, and was found to contain teeth, hairs, and foul-smelling sebaceous material Death occurred from heart failure 2 days later

Figs 24 and 25 show the characteristic location in the anterior mediastinum These radiograms are from a woman aged 27 who was completely symptomless, the intrathoracic tumour being discovered during a mass radiography survey of the employees of the firm for which she was working as a radio-operator When seen at Brompton in November 1944 the radiologist reported the X ray appearances as consistent with a calcified dermoid cyst Subsequent radiograms taken up to October 1946 showed no material change in comparison with those seen in the original film The question of a possible chondroma arising from a rib was discussed, but the position of the tumour in the anterior mediastinum and the absence of any change in its radiological characters over a long period of time was regarded as in favour of the diagnosis of a dermoid cyst which had undergone calcification

Figs 26 and 27 show a similar tumour, situated posteriorly, thought to be a calcified dermoid This patient was examined by a mass radiography unit The first X-ray at Brompton was made on May 8th 1943 The patient, a man of 50, was again X-rayed on September 18th, when no appreciable alteration was observed in the size of the tumour

Figs 28 and 29 are of particular interest from the standpoint of differential diagnosis and as illustrative of the practical impossibility in many cases of arriving at a certain conclusion as to the exact nature of what radiologically appears to be a benign growth This patient, a married woman aged 32 was admitted to Brompton for investigation on May 24th, 1944 with a note from the Director of a radiotherapy centre in the provinces who had seen her on account of an attack of haemoptysis about 2 months previously and had discovered a mass situated in the region of the right anterior mediastinum but which he thought was probably intrapulmonary, presumably because of the history of bleeding He suspected the possibility of malignancy, despite the sharply defined edge of the tumour, and as it appeared to be fairly well localized he suggested that it might be a peripheral type of bronchial carcinoma that would prove to be operable The whole clinical history of this case is so remarkable that I feel it is worth recording in detail

On admission she gave a history of having been in good health up to October 1943, when she suddenly coughed up a small amount (about a drachm) of blood Prior to this she had not noticed any cough, but ever since this incident cough had been more or less continuous In January 1944 she had another slight haemoptysis and was complaining of cough and dyspnoea on exertion On examination she was found to have mitral stenosis The heart was not enlarged, but there was an unmistakable pre systolic murmur localized



Fig 26 Calc fied dermo d



Fig 27 Same case as Fig 26 left lateral view

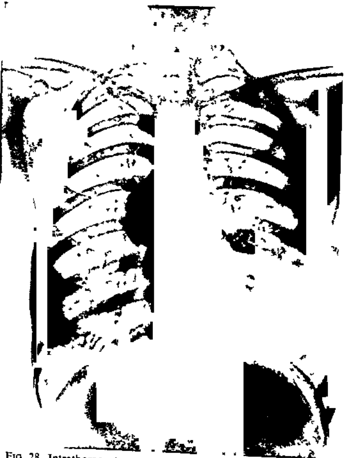


Fig 28 Intrathoracic tumour erroneously diagnosed as a dermoid



Fig 29 Same case as Fig 28, right lateral view Showing anterior position of tumour

to the apex There was no X-ray evidence of auricular enlargement The electrocardiogram showed normal curves in leads I, II, and III There was no clinical evidence of congestive failure She was kept in Brompton until June 18th and discharged home, her symptoms being appreciably less after the 25 days of complete rest The following report was sent to her regular medical adviser

The X rays of this patient s chest showed a shadow which I took to be a primary benign tumour, *possibly a dermoid* situated anteriorly on the right s de I did not think this was the cause of her haemoptysis which I attributed to slight pulmonary congestion secondary to mitral stenosis The heart lesion is a slight one and I think not progressive She has improved considerably with rest I thought a third pregnancy would be likely to upset her very badly and I advised her strongly to take precautions against such an occurrence In ordinary times I should probably have asked one of my surgical colleagues to see her in regard to the tumour of the lung I do not think this is likely to cause trouble in the immediate future but I should like to see her again and X ray her to see if it has increased in size If this is happening it may eventually cause pressure symptoms and give rise to trouble at the moment I do not think there is any urgency in the matter

Her second child was born in July 1944 and she seems to have kept reasonably well, though there were recurrent slight attacks of blood spitting In December she was again seen at Brompton in the out patient department and the whole matter was reviewed X-ray examination showed no increase in the size of the tumour, but she appeared to be rather more breathless She was then seen by one of the surgeons, who advised that she should be admitted with a view to removal of the tumour after adequate preparation On May 16th, 1945 an exploratory thoracotomy was performed The tumour was easily seen, it was about the size of an orange The pleura was incised and the mass was freed from the superior vena cava and surrounding tissues of the anterior mediastinum and removed During the operation the patient s breathing was observed to be stridorous, and after removal of the mass and while the wound was being closed the anaesthetist passed a bronchoscope and saw a small endobronchial growth, overlying the carina A portion of this was removed for biopsy and the patient was taken back to the ward

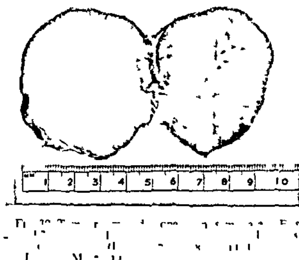
The histological report on the biopsy specimen was as follows

There is a considerable amount of necrotic débris in the material sent for examination In addition there is a portion of the tumour The cells are large with irregular deeply staining nuclei and frequent mitotic figures There is a tendency to acinar formation in the tumour but there is no mucin secretion *The tumour appears malignant an l seems to be a poorly differentiated adeno-carcinoma*

A subsequent report on the main mass removed from the chest was as follows

The tumour is the size and shape of a duck s egg The cut surface shows a firm white appearance similar to that of Hodgkin s disease Sections of the mass show an obvious

reticulosis There is hyperplasia of the reticular cells and an excessive number of lympho cytes There is no increase in the number of eosinophiles and no giant-cell formation There is however, a marked tendency to fibrosis of the type seen in late Hodgkin s disease The appearances are those of a mixed reticulosis of the kind formerly described as atypical Hodgkin s disease



It was evident that the malignant endobronchial growth was independent of the intrathoracic tumour In view of the histological character of the former this patient was transferred to the Royal Cancer Hospital for radiotherapy Treatment was begun on June 21st and completed on August 7th (4 900–4 300 r) When seen again on October 12th she was thin and pale but there was no cough or dyspnoea nor had she had any further haemoptysis No enlarged lymph nodes were palpable

This patient died on February 24th 1946

One other case may be quoted as important from the standpoint of differential diagnosis Figs 31, 32, and 32 A show the X ray appearances in a middle aged man whom I saw in consultation on account of some breath lessness and general debility From the radiological characters and especially from the anterior position of the tumour we concluded that this growth was in all probability a dermoid and operable Mr Vernon Thompson who was asked to see the patient with a view to surgical treatment was unwilling to commit himself to a diagnosis of dermoid cyst but agreed that exploratory thoracotomy was indicated At the operation the tumour was found to be an *inoperable carcinoma*



FIG. 31. Intrathoracic tumour diagnosed clinically and radiologically as a dermoid, but found on exploration to be a carcinoma.



FIG. 32. Same case as Fig. 31, lateral view. Showing anterior position of tumour.

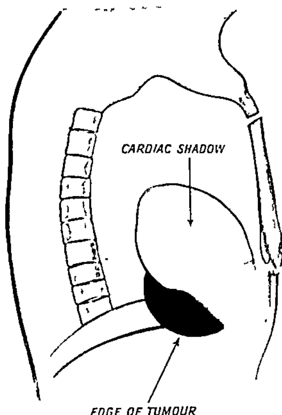


FIG 32 A Diagram explanatory of Fig 32

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IV

NEUROGENIC TUMOURS

The neurogenic tumours form a more or less definite group among the tumours with which the thoracic surgeons have had to deal, and which, though by no means common, are appearing with increasing frequency in the literature of chest disease A certain amount of difficulty may be experienced by students of this subject on account of the complexity of nomenclature with which it has been surrounded The existence of tumours of neurogenic origin has long been known, those arising from nerve tissue (true neuromata) being rare and met with chiefly in connexion with the sympathetic system, those arising in the nerve sheath (sometimes called false neuromata) being of commoner occurrence and found in various parts of the body The false neuromata consist of nerve-fibres with varying amounts of connective tissue in between They may be single or multiple the best known example of the latter is seen in the condition known as multiple neuro-fibromatosis (von Recklinghausen's disease) which is characterized by widespread superficial tumours of this type in connexion with the skin, occasionally associated with deeper growths of similar nature in the viscera

The histological variations of single tumours arising from the nerve sheath have been described of late by Geschickter, who separates them into two main groups The first and more highly differentiated of these consist largely of fibrous tissue with considerable amounts of collagen, and exhibit a characteristic disposition of the nuclei, which tend to aggregate in several areas of the growth in a so-called 'palisade' arrangement Tumours of this type, which have been referred to as 'neurinomas', neurilemmomas , or 'perineural fibroblastomas', are regarded as benign in character, and according to Geschickter rarely if ever undergo malignant changes The second, less differentiated, group are liable to undergo malignant changes, and may recur after removal, they have been variously described as myxoid neuromas', 'fibromyxomas', or fibroneuromas'

The solitary intrathoracic tumour commonly referred to as a neuro fibroma is ordinarily classed among the benign tumours, and the practical experience of thoracic surgeons, at any rate in symptomless cases which have come into their hands at a comparatively early stage, would seem to justify this A recent review, however, by Kent, Blades Valle, and Graham has made it clear that the proportion of cases in which malignant change occurs in these tumours is considerably higher than has been hitherto supposed In their analysis of a series of 105 cases collected from all the literature they find

malignancy in 37 per cent, and of their own series of 21 additional cases (18 proved intrathoracic nerve tumours and 3 probable but unproved neurogenic tumours) over 40 per cent were found malignant Their figures from the Barnes Hospital are given in tabular form as follows

TABLE IV *Malignant Change in Neurogenic Tumours* (Kent *et al*)

No of cases		*Percentage*
Benign	10	47 6
Malignant	9	42 8
Questionable	2	9 5
Total	21	99 9

They also give a table of the cases collected from the literature

TABLE V *Malignant Change in Neurogenic Tumours Cases Collected from the Literature* (Kent *et al*)

No of cases		*Percentage*
Chest wall tumours		
Malignant	24	88 8
Benign	3	11 2
Total	27	100 0
Mediastinal tumours		
Malignant	15	20 3
Benign	59	79 9
Total	74	100 2

As a corollary to these observations they add the warning that 'there is no justification for the all too common opinion of the medical profession that *suspected nerve tumours of the thorax do not require operation unless or* until pressure effects have been noted', and they go on to urge their colleagues to accept a presumptive diagnosis of intrathoracic neuro fibroma as a sufficient indication for thoracotomy as soon as possible

Location. It is a matter of general experience that these tumours are almost invariably situated in the posterior part of the thorax, usually arising in the paravertebral gutter Kent and his colleagues found this to be the case in 19 out of the 21 cases reported in their own series, the remaining 2 being in the anterior mediastinum They note that in some cases the growth arises *within one of the intervertebral foramina* (*vide* Case 2, E W) and extends inwardly to the spinal cord and outwardly to the paravertebral sulcus Such growths have often been described as 'hour-glass' or 'dumb-bell' tumours

D'Abreu in a report of 8 cases under his care notes that 4 of these were situated characteristically in the posterior mediastinum, 2 in the lateral aspect

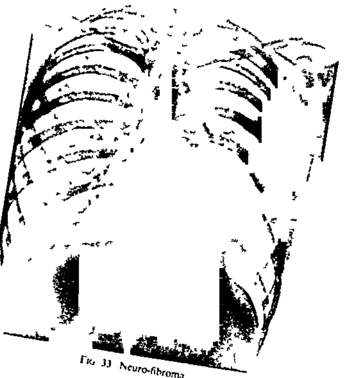


Fig 33 Neuro-fibroma



Fig 34 Same case as Fig 33, lateral view



Fig 35 Same case as Fig 33, oblique view



Fig 36 Same case as Fig 33, after induction of a diagnostic pneumothorax

of the chest, and only 1 in the anterior mediastinum The latter situation he regards as extremely rare and this example he thinks may be unique

Clinical and Radiological Features. I have already indicated that in many cases the condition is symptomless, the growth being discovered as a result of routine X-ray examination In others there are slight symptoms due to pressure on a nerve, the pain being quite often referred along the course of one of the intercostal nerves In advanced cases, in which the growth has attained a considerable size, there may be severe pressure symptoms such as dysphagia, dyspnoea, and even stridor with cyanosis Horner's syndrome from involvement of the sympathetic has been described Some cases, with intraspinal extension, may present with a compression paraplegia

Radiologically neurogenic tumours appear as rounded opacities with a sharply defined edge similar to the shadows cast by many other non-malignant tumours, from which it may be, and indeed frequently is, impossible to distinguish them by the radiographic appearances alone Twining has noted widening of the intercostal space corresponding with the situation of the tumour with slight elevation of the rib above it in some cases he describes erosion of the vertebral end of the rib and transverse process with enlargement of the intervertebral foramen and narrowing of the pedicles The distinction between a neurogenic tumour and a dermoid usually rests upon the position (anterior or posterior) shown by the lateral radiogram, but as I have already hinted this though of no little significance is not an infallible guide (cf Fig 21, Chap III) A substernal thyroid may be mistaken for a neurogenic tumour, and the pre-operative diagnosis if established will in all probability rest upon a synthesis of other observations in addition to the purely radiological evidence A good example of the difficulty of exact diagnosis of these tumours is seen in Fig 44 (Chap V) in which the radiological appearances are very similar to those of the neurogenic tumours

I have spoken in general terms of the question of potential malignancy The significance of this can be better appreciated by reference to the following cases which illustrate this point in addition to the clinical and radiological picture of the condition as it presents itself in actual practice

Case 1 J H a boy aged 12 had had an attack of bronchitis and since his recovery was somewhat slow his medical adviser called in a consultant who suggested that an X ray examination was advisable This revealed a mass in the left side of the chest (see Fig 33) Prior to the attack of bronchitis there had been no history of any respiratory disability and the boy s general health had been perfectly good The radiologist reported (24 2 41) Heart shadow projected to the left (apparently due to posture) There is a rounded shadow in the left middle and lower zones lying posteriorly (Figs 34 and 35) A barium swallow showed no oesophageal abnormality and no herniation of the stomach or intestines and the radiologist observed if an encysted effusion or a hydatid seem clinically unlikely the presence of a fibroma may be considered Fig 36 shows a radiogram taken (17 3 41)





Fig 37 Neuro fibroma

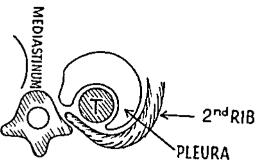


Fig 38 Same case as Fig 37 Diagram showing position of tumour seen at operation

after induction of an artificial pneumothorax as a preliminary to thoracotomy Exploration of the chest was undertaken (18 3 41) an incision being made in the 8th left interspace, the posterior ends of the 8th and 9th ribs being resected A large extra pulmonary tumour, the size of a grapefruit was seen The pleura was incised and the growth was gradually dissected out Medially it was insinuating itself between the aorta posteriorly and the oesophagus anteriorly Posteriorly especially in its lowest part it was penetrating into the chest wall There was one prolongation of the tumour passing through the 6th intervertebral foramen Recovery after the operation was uneventful

The pathological report on the specimen (2 4 41) was as follows 'The histological appearances reveal a neuro fibroma with sarcomatous changes' [sic] The patient was discharged from the Brompton Hospital on April 20th 1941 and in view of the above report on the section was given a precautionary course of deep X ray therapy

A recent inquiry was received at Brompton from an insurance company asking for details of the previous medical history of this boy who now after an interval of 7 years appeared to be in perfect health and was submitting a proposal for life insurance on the ordinary terms

Case 2 E W a young married woman aged 27 was admitted to Brompton in January 1937 with a history of pain in the right shoulder and forearm which had been troubling her on and off for about 9 years An operation for cervical rib had been performed in 1934 but the pain had persisted On admission X-ray examination showed a rounded opacity in the upper zone of the right lung (Fig 37) which was thought to indicate a neuro fibroma no deficiency of vertebrae was observed Thoracotomy was performed on January 13th and the tumour was removed it was extra pleural and was lying in the costo-vertebral angle The attached diagram (Fig 38) is reproduced from a drawing made in the operating theatre at the time

Recovery was uneventful Microscopic examination of the growth showed it to be composed mainly of fibrous tissue

Case 3 J G a man aged 34 consulted his doctor on account of pain in the dorsi lumbar region Clinical examination revealed no abnormality but a radiogram of the chest showed a circumscribed opacity on the right side situated posteriorly which was thought to be indicative of a neuro fibroma The 9th rib (posteriorly) appeared to be eroded (Figs 39 and 40)

He was admitted to one of the surgical wards at Brompton on June 5th 1942 when he gave a history of constant nagging pain in the back over a period of many years He was found on examination to have a definite scoliosis to which in the past his pains had presumably been attributed No localized tenderness of the spine was detected Thoracotomy was performed on July 1st after a preliminary artificial pneumothorax A postero-lateral incision was made in the 8th interspace and the lung was retracted A dumb-bell tumour was discovered situated in the costo vertebral sulcus and measuring about 4 inches in diameter The tumour was extra pleural The 9th and 10th ribs were eroded The mass was freed and the pedicle cut at the intervertebral foramen Removal of the growth was uneventful and the patient made a satisfactory recovery and was discharged home on August 14th

The pathological report on the growth (Fig 41) was as follows

Section shows a neuro-fibroma The growth is not very cellular much hyaline fibrous tissue being present No evidence of malignancy or other important change was noted in the specimen examined



Fig 39 Neuro fibroma

Fig 40 Same case as Fig 39 after induction of a diagnostic pneumothorax

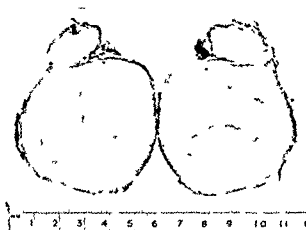


FIG 41 Neuro-fibroma removed at operation Same case as Fig 39
(Photograph of specimen in the Brompton Hospital Museum)

These 3 cases are quoted as fairly representative examples of neuro-fibromata with *successful and uncomplicated surgical treatment* The following case forms an interesting comparative study

Case 4 T W F a man aged 38 had attended as an out patient at one of the smaller London hospitals for 3½ years a diagnosis having been made of growth probably neuro-fibroma involving the 4th dorsal nerve He was referred to Brompton by his physician because for the past year the tumour had definitely increased in size and the question of its removal by a surgeon had been under consideration He was admitted to Brompton in February 1945 X ray examination showed a rounded opacity spreading outwards in the left upper zone of the chest (Fig 42) and situated posteriorly (Figs 43 and 43 A) The suggested diagnosis was neuro-fibroma Thoracotomy was performed on February 14th after preliminary induction of pneumothorax The tumour which was felt to be mainly solid though cystic in part was removed without undue difficulty There appeared to be some erosion of the 7th rib Recovery from the operation was uneventful

The pathological report was as follows

> The specimen is a spherical tumour with central degeneration and haemorrhage Sections show a fibro-sarcoma with a large amount of interstitial tissue In some areas there is a tendency to palisade arrangement of the cells suggesting that the tumour may be derived from neurilemma Mitotic figures are uncommon but multinucleate giant cells are fairly frequent *This growth is probably one of low-grade malignancy*

In view of the above report prophylactic X ray therapy was arranged for this patient who left Brompton on April 5th

Later on he developed abdominal symptoms, thought to be due to duodenal ulcer Eventually in the spring of 1946 he was taken into one of the big teaching hospitals in London where an exploratory laparotomy revealed an inoperable carcinoma of the stomach. He had had no further symptoms referable to his original intrathoracic lesion

I have quoted the above case especially in relation to the observations of Kent and his colleagues in regard to the proportion of neurogenic tumours which show malignant or potentially malignant features The actual cause of death in this case appears to have been a gastric carcinoma It is not suggested that there was any direct relation between this and the intrathoracic tumour

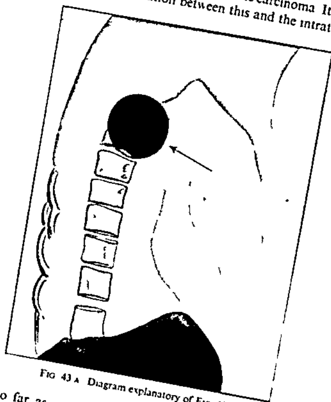


FIG 43 A Diagram explanatory of Fig 43

from which so far as our information goes, the man suffered no further symptoms after its removal

Malignant change in the tumours found in von Recklinghausen's disease have been recorded on numerous occasions Such a case is quoted by Louria and others of a young woman with generalized neuro-fibromatosis, the lesions appearing in the first place on the forehead and chin and later in various parts of the body Laparotomy undertaken because of abdominal and lumbar pain, disclosed two retroperitoneal masses which were removed and which proved on section to be neuro-fibromata Still later this patient developed a (?) pleural effusion on the left side, and X-ray examination showed a circumscribed circular shadow in the right upper zone of the chest When this patient

eventually died, autopsy revealed a large lobulated friable mass filling the left side of the chest and practically replacing the lower lobe of the left lung In the right upper lobe was found a circumscribed mass measuring 4½ cm in diameter Pathological examination and section of these lung lesions showed a spindle-cell sarcomatous growth The skin lesions appear to have been typical neuro-fibromata

It will be noted that all the foregoing descriptions relate to extra-pulmonary tumours Primary neurogenic tumours of the lung itself appear to be extremely rare One extremely interesting example has been reported by Bartlett and Adams They describe a case of a neurinoma which they believe to be the first recorded instance of surgical removal of a solitary primary neurogenic tumour of the lung

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V

RARER FORMS OF BENIGN TUMOURS

(LIPOMATA, CHONDROMATA, OSTEOMATA, FIBROMATA, ANGIOMATA, ETC)

THE present chapter represents an attempt to give a brief but comprehensive account of a variety of non malignant tumours within the chest which, though more or less capable of division into groups according to their main histological characteristics, do not always permit of hard and fast pathological classification, since in not a few cases microscopic examination reveals more than one type of tissue The predominance of one or other variety of tissue cells has in practice tended to decide the nomenclature of the tumour in question, but occasionally the appearance of cells of different type in the same tumour has resulted in a resort to various hybrid descriptions This has, perhaps, been responsible for a certain amount of confusion in the minds of those who seek, not unreasonably, for a clear-cut picture of the morbid anatomy of any growth which they may be called upon not merely to diagnose but also to treat Lipomata, for example, are by their very name, to be regarded as fatty tumours but the histological combination of fibrous tissue with fat cells may sometimes give rise to a diagnosis of fibro-lipoma in a benign growth, the precise nature of which, neither clinical nor radiological evidence prior to operation has enabled one to determine (cf p 57) The same applies to the chondromata which though obviously consisting mainly of cartilaginous tissue, may show areas of calcification or of ossification, the islets of cartilage being in some instances separated by vascular connective tissue with occasional areas of adipose tissue Not a few hybrid descriptions such as 'chondrosarcoma', fibro lipo-sarcoma', &c, are to be found in the literature in reference to intrathoracic tumours which have exhibited the clinical and radiological phenomena associated with growths of non malignant character in the ordinary sense of the word and which have been successfully removed by the surgeon Subsequent histological reports on which the published diagnosis has rested have indicated not only the polymorphic character of the growth, but also, presumably, its malignant potentialities in comparison with other tumours of simpler histological structure It is of some importance that this aspect of the subject should be mentioned, if only for the sake of clearness With this brief preliminary reference we may now consider the general characteristics and the broad diagnostic features of those rarer forms of thoracic neoplasms which come under the above heading

LIPOMATA

So far as I can ascertain, the first record of a case of thoracic lipoma was published in 1783 by Fothergill These tumours are undoubtedly among the rarest of the benign intrathoracic growths This is clear from a review of the literature in 1930 by Yater and Lyddane In 1934 a report of the Chest Tumour Registry by Andrus showed the number of recorded cases at that time to be 16 By 1940 this had increased to 34 (McCorkle, Koerth, and Donaldson) A recent paper by Smart and Vernon Thompson (1947) gives the total number up to date as 39 In view of the increasing activity of all thoracic surgical centres it is likely enough that more cases will continue to be recorded from time to time, but sufficient has been said to indicate the rarity of this condition

One of the best reviews of the subject is that of Heuer, whose paper is widely quoted by other authors, and who has conveniently suggested the division of thoracic lipomata into three main groups This is a good practical classification which is generally recognized and adopted The first group comprises tumours which lie partly within, partly outside the chest, the intrathoracic and extrathoracic portions being connected by a narrow isthmus occupying a perforation in the chest wall (the so called hour-glass type of tumour) In the second the tumour is situated mainly in the mediastinum, but extends upwards into the neck Finally there is a group in which the tumour is wholly intrathoracic These growths vary considerably in size and may eventually reach enormous proportions, the greatest recorded weight being 17½ lbs (Leopold), though sometimes the patient may be fortunate enough to have an exploratory operation at a comparatively early stage, when the tumour still offers a reasonable prospect of removal without undue difficulty

Morbid Anatomy, &c. The intrathoracic lipomata are believed to originate from extra-pleural fat, i e from adipose tissue situated at various points in the subpleural region According to Ewing it is not uncommon to find a localized overgrowth of adipose tissue in the mediastinum, especially in obese patients and in those addicted to alcohol When tumours thus originating attain an appreciable size they may extend into the pleural cavity or along the inter costal spaces If the growth makes its way through the chest wall, it may present externally on the front of the chest, below the breast or elsewhere, or at the back The purely intrathoracic tumours would appear to constitute the majority of cases In Heuer s series of 29 lipomata, 17 were of this variety (58 6 per cent) The remainder fell into the first two groups, i e the hour-glass type, and the intrathoracic growths which extended into the neck Histologically they may consist almost entirely of fat cells, though, as we

have already observed, it is not uncommon to find other types of tissue, fibrous, myxomatous, &c, associated, the ultimate diagnosis depending on the prominence of one or other histological variety Diagnosis of a lipoma prior to actual exploration and pathological examination is nearly always a matter of uncertainty In one case recorded by Walker an enormous mass, measuring 18 5 by 8 by 7 cm, was enucleated in two successive operations The pre-operative diagnosis had been 'mediastinal dermoid', but on exploration the mass proved to be a fatty tumour, portions only of which were removed at the first operation At a subsequent operation it was found that the growth had broken down and partly liquified, and 1 47 kg of fatty bits were removed The patient improved for a while but subsequently died from cardiac failure, presumably associated with the gross mediastinal displacement caused by a tumour of such considerable size

Diagnosis. It is probably very seldom that a positive diagnosis of lipoma is made in a patient in whom the clinical and radiological findings indicate the presence of an intrathoracic neoplasm until the tumour has actually been removed by the surgeon and submitted to scrutiny by the pathologist The *clinical symptoms* depend, as in the case of other benign tumours, on the size and position of the mass and its anatomical relation to other structures within the chest In the great majority of cases the existence of such a growth is undetected in the early stages, when surgical removal is a comparatively easy undertaking, it is not until the mass has attained sufficient size to cause obvious pressure symptoms that the patient is led to seek medical advice Moreover it must be remembered that if the rate of growth is very slow, as is often the case, a tumour of this kind may reach surprising dimensions before causing manifest symptoms, so great is the capacity of the body to adapt itself to gradually changing conditions The most frequent symptom is gradually increasing dyspnoea Cough, hoarseness (from involvement of the laryngeal nerves) cyanosis, and oedema (from direct cardiac embarrassment) may occasionally be seen The physical signs in the chest likewise vary according to the position and size of the intrathoracic mass Dullness to percussion in some part of the chest is the most obvious and frequent physical manifestation If the tumour projects into the neck or through the chest wall, the possibility of pre-operative diagnosis is somewhat greater Radiologically the evidence is that of an intrathoracic tumour, and the appearances seen in a standard film can hardly be said to show anything specifically characteristic of lipoma in contradistinction to any other non-malignant tumour of the thorax

Two points may be mentioned to which attention has been drawn in the literature Heuer in discussing his own contribution to the records has referred to a certain transparency in the edges of the shadow thrown on the

film by a lipoma, which he regards as somewhat distinctive and which is not shown by a large collection of fluid, or presumably by other neoplasms Another radiological feature which has been emphasized by several authors is the appearance of lobulation in the shadow of the growth Walker lays some stress on this, and Barrett and Barnard have also referred to it in connexion with a case recently recorded by them This was an unusual thoracic tumour in a boy of 4 from whom an intrathoracic lipoma was successfully removed The pre-operative investigations in this case were very comprehensive X-ray examination and physical examination revealed the presence of a 'solid or fluid space-occupying lesion' [*sic*] in the front of the left chest, the heart being grossly displaced towards the right side A barium swallow showed that the mass was well in front of the oesophagus Bronchoscopy showed displacement upwards and outwards of the left lower lobe bronchi but no intrabronchial abnormality The authors note that the edges of the shadow were a little irregular '*as though the mass were lobulated in places*' (my italics) They observed that the most likely diagnosis was mediastinal tumour, but noted that of the various possibilities that of a teratoma or a benign tumour such as a lipoma was suggested by the lobulated outline

In one case of removal of a mediastinal lipoma Watson and Urban established the diagnosis before operation Reliance was placed upon history and physical signs, and upon the X-ray appearances including the 'contrast visualization' afforded by injection of 35 c c of a 70 per cent solution of diodrast into one of the antecubital veins, the X-ray films being exposed 2 seconds and 4 5 seconds respectively after beginning the injection Such contrast visualization is undoubtedly of the greatest practical value to the surgeon in determining the relations of any tumour which it is proposed to explore I must confess, however, that it is difficult to see how it can afford a differentiation between a lipoma and any other relatively solid tumour within the chest

Apart from the clinico-radiological picture there is one other point to which reference has been made, viz the results of exploratory puncture Walker in his preliminary investigation of a very large mediastinal lipoma in a boy of 13, notes that on puncture of the chest the needle 'entered a soft mass without resistance' In his commentary on this case he emphasizes this and seems to attach some importance to the different feeling of resistance to the needle in a dermoid, for example, in contradistinction to a fatty tumour in the former there is considerable resistance, whereas in the latter the needle passes forward easily, once its point is within the actual tumour

I have drawn attention to the above points in diagnosis for the guidance of those who are concerned with the treatment of such conditions, more in the desire to record any suggestions put forward by experienced team-workers,

since they are likely to be helpful, than with any feeling that the exact nature of a benign tumour within the chest can ever be determined with certainty until it has actually been exposed and examined

FIBROMATA

Pure fibromata are, perhaps, the least common of all the intrathoracic tumours Roberts in a discussion at the Royal Society of Medicine in 1926

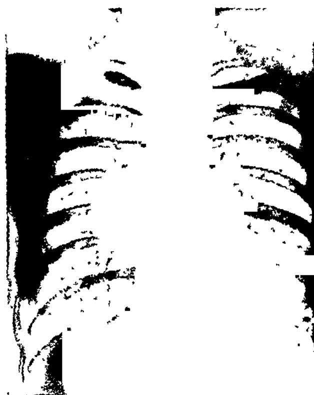


FIG 44 Fibro-lipoma (diagnosed before operation as a neuro-fibroma)

referred to 6 cases of benign tumours in his own experience during the preceding 6 years, of these only 2 were described as fibromata Blades in a more recent survey found only 32 cases of mediastinal fibroma in the literature up to October 1941 Harper (1939) quotes 9 examples of such growths arising from the thoracic wall Of two examples which I have recorded elsewhere (Davidson, *Pract Man of Dis of Chest*, 3rd ed , 1948, pp 578 and 583) the exact histological details are lacking, though clinically and radiologically the



FIG 45 Same case as Fig 44, right lateral view Showing posterior position of tumour



FIG 46 Fibro lipoma removed at operation Same case as Fig 44 (Photograph of specimen in the Brompton Hospital Museum)

tumours were thought to be fibromata In both these patients the tumour had grown to huge dimensions and almost completely filled one side of the chest In one case an attempt was made to shrink the growth by insertion into it of radon seeds, but although some diminution in size was obtained, it was still found impossible to remove it surgically In the other case the tumour was removed, but the patient died three hours after the operation A successful case is reported by Clagett and Hausmann who removed a huge intrathoracic mass which was found to consist of mature fibroblasts with considerable amounts of collagen This tumour showed no histological characters suggestive of malignancy

Clinically these tumours are manifested by gradually increasing dyspnoea, which may eventually be accompanied by other associated pressure symptoms Radiologically they appear usually to be situated posteriorly

The following case may with advantage be cited here as an example of the difficulty frequently encountered in the pre-operative diagnosis of benign intrathoracic tumours The patient was an unmarried lady of 43 She consulted her regular medical adviser on account of a slight cough, about which she was anxious because her sister, whom she had been looking after during the previous 3 months had died of pulmonary tuberculosis The doctor found nothing abnormal on physical examination of her chest, but had an X-ray examination which showed the appearances seen in Figs 44 and 45 He sent her to me for an opinion on the nature of the tumour shown in the radiograms, and for advice as to treatment He added that, apart from the slight cough, the patient had had no symptoms and that her general condition had given no cause for anxiety On examination I found no abnormal physical signs The X-ray appearances were suggestive of the presence of a benign intrathoracic growth and she was advised to undergo an exploratory thoracotomy This was performed on September 5th, 1948 under general anaesthesia with 15 mg of curara The postero-lateral approach was adopted, with incision through the 8th intercostal space and division of the 8th rib On opening the pleural cavity the tumour was disclosed, wedged in the paravertebral groove It was thought to be a neuro-fibroma with a narrow base of attachment It was difficult to say whether it arose from an intercostal nerve *or from the sympathetic chain*

Recovery was uneventful and the patient was discharged home on October 4th

Pathological examination showed a well capsulated tumour the cut surfaces showed a firm fibrous surface with many yellowish areas Histological examination failed to show any ganglion cells, the picture being that of a benign fibroma There were many focal lymphoid aggregates which were generally in the neighbourhood The yellowish areas contained fat cells,

which were of normal type and not the result of inflammatory degeneration The tumour was therefore regarded as being a fibro-lipoma

Before the operation, a provisional diagnosis of neuro fibroma had been made The opinion of the radiologist was that if the growth in the right side of the chest was extra-pulmonary, it was most likely to be a neuro-fibroma Bronchoscopic examination, prior to the thoracotomy, showed no abnormality in the bronchial tree

CHONDROMATA AND OSTEOMATA

The occurrence of tumours composed of cartilaginous tissue in various portions of the respiratory tract has been recognized for many years, but like others mentioned in this chapter they must be included among the rarer forms of new growth that are found within the chest Multiple chondromata of the lung, situated at the hilum, within the lung parenchyma, and on the surface of the pleura, were described by Virchow These growths, while frequently composed of pure cartilage, may undergo changes and eventually show calcareous foci or in some instances become ossified One of the best reviews of the literature of the subject is that of Hickey and Simpson, who analysed the reports of 38 cases of alleged chondroma of the lung, to which they added a complete account of 2 cases of their own They inclined to the view that the incidence of thoracic chondromata was greater than was indicated by the comparatively scanty publications available on the subject

I have referred to the entire group of chondromata of the respiratory organs as rare growths It would appear, however, that the most infrequent of all are those situated within the bronchus, the pulmonary chondromata being far commoner in comparison In Hickey and Simpson's account which is entitled 'primary chondroma of the lung' there is a tabulated abstract of 38 cases (excluding their own 2 cases), some of which, however, would appear from the description to be chondromata originating from a bronchus Wilks's chondroma seems to have had such an origin Chiari describes 2 cases in both of which a nodular growth was found in a bronchiectatic cavity Feller records a chondroma the origin of which (lung or bronchus) seems doubtful since bronchi were found penetrating into the tumour, and in the case described by Caussade, Surmont, and Lacapere, the origin of the growth appears to have been bronchial rather than pulmonary The remainder mentioned in the analysis were apparently true pulmonary chondromata In a report already published by me (loc cit) of a purely cartilaginous endobronchial tumour attention is called to the extreme rarity of this condition A short account was given by Siegert in 1892 with references Von Eicken in 1907 removed a benign enchondroma from the bronchus of a man aged 41, and Blecher (1910) reports a large chondroma arising from a bronchus The

Jacksons in their monograph on bronchoscopy &c mention enchondromata and osteo-chondromata among a large variety of tumours of the bronchial tree of which they have had personal experience

One of the most unequivocal accounts of a primary chondroma of the lung is that recorded by Lakin as long ago as 1912 This was a case of a woman of 53 who died from multilobular cirrhosis of the liver The post mortem findings were such as are usual in this disease except for the fact that one *circumscribed nodule in the liver just below the thickened capsule projected* above the surface of the organ and was so hard that it was impossible to cut through it with the knife On examination of the chest a firm nodular mass was found near the hilum of the left lung and in view of the possibility of the hard mass in the liver just mentioned being malignant it was suggested that the intrathoracic nodule might be a secondary carcinomatous deposit No other tumour however was found in the lungs or in any other part of the body and this nodule on section showed *the typical bluish translucent appearance* commonly associated with cartilage Microscopic section showed it to consist of hyaline cartilage which was for the most part sharply delimited from the surrounding lung tissue In some places there was evidence of myxomatous change This then was proved to be a pure primary chondroma of the lung It is interesting to note that the author observes that up to that time only four examples of the condition had been brought to the notice of the Pathological Society of London in all the fifty eight years of its existence

Fig 47 shows a specimen of a cartilaginous tumour This is a firm more or less spherical mass about 5 5 cm in diameter situated in the lower part of the right upper lobe The gross specimen was extremely hard and had to be cut with a saw

Microscopic examination of this specimen showed that the tumour was composed of large irregular masses of cartilage between which in some areas were narrow clefts These clefts were lined by bronchial epithelium There were also some small areas of mucin secreting cells

Fig 48 shows a spherical tumour about 2½ inches in diameter sharply demarcated from the surrounding lung tissue

The microscopic section showed that the growth was composed of well differentiated mucin secreting glands The glandular acini were extremely regular many of them were secreting mucin The histological diagnosis was benign hamartoma (Fig 49)

In recent literature the expression hamartoma has frequently been used in connexion with these cartilaginous growths and may demand some explanation The word was originally employed by Albrecht to denote certain tumours in which there was found an abnormal admixture of the normal components of the organ in question and since his description of the general

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CHONDROMATA AND OSTEOMATA

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Fig 47 shows a specimen of a cartilaginous tumour This is a firm, more or less spherical mass, about 5 5 cm in diameter, situated in the lower part of the right upper lobe The gross specimen was extremely hard and had to be cut with a saw

Microscopic examination of this specimen showed that the tumour was composed of large irregular masses of cartilage, between which, in some areas, were narrow clefts These clefts were lined by bronchial epithelium There were also some small areas of mucin-secreting cells

Fig 48 shows a spherical tumour, about 2½ inches in diameter, sharply demarcated from the surrounding lung tissue

The microscopic section showed that the growth was composed of well differentiated mucin-secreting glands The glandular acini were extremely regular, many of them were secreting mucin The histological diagnosis was 'benign hamartoma' (Fig 49)

In recent literature the expression 'hamartoma' has frequently been used in connexion with these cartilaginous growths and may demand some explanation The word was originally employed by Albrecht to denote certain tumours in which there was found an abnormal admixture of the normal components of the organ in question, and since his description of the general

which were of normal type and not the result of inflammatory degeneration The tumour was therefore regarded as being a fibro lipoma

Before the operation, a provisional diagnosis of neuro-fibroma had been made The opinion of the radiologist was that if the growth in the right side of the chest was extra-pulmonary, it was most likely to be a neuro fibroma Bronchoscopic examination, prior to the thoracotomy, showed no abnormality in the bronchial tree

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group of hamartomata the expression has been adopted in the description of cartilaginous lung tumours in particular Hickey and Simpson in their commentary have expressed the view that the so-called pulmonary chondromata are growths which have their origin in aberrant bronchial *anlagen* [*sic*] since it appears to them that all the structures which are found in these (frequently)



Fig 47 Chondroma of Lung (Photograph of specimen in the Brompton Hospital Museum)



Fig 48 Hamartoma of Lung. (Photograph of specimen in the Brompton Hospital Museum.)

mixed tumours are normally found in bronchi It is in the light of this conception that the expression hamartoma (ἁμαρτάνειν, *to fail, to miss the mark*) has come to replace the original designation, chondroma

The existence of tissue elements other than cartilaginous is mentioned in a report by McDonald, Harrington, and C study of 23 cases, in 3 of which the tumour was removed by vth in t 20 having been found at autopsy, these 2C a of 7,972 post-mortem the on es being thus 0 25 per cent) ng of pure chondromata of the d consider that those in other tissues such as chondromas, despite the

Simon and Ballon record a very large and unusual hamartoma (so-called chondroma) of the lung which, though from many aspects the growth appeared to be benign in character, yet showed some areas which were histologically suggestive of malignancy There seems little doubt that the tumour they describe was a primary lung tumour unconnected with the bronchi, although a bronchus was found to be 'riding over it' [*sic*]



FIG 49 Microphotograph of the specimen shown in Fig 48 (benign hamartoma)

Diagnosis There are no features clinical or radiological which can be regarded as pathological of this condition These growths do not as a rule attain such a size as to give rise to gross pressure symptoms, nor is there anything in the radiological picture of a chondroma of the lung that would infallibly distinguish it from any other benign tumour In Hickey and Simpson's cases the areas of calcification shown in the radiograms were suggestive, but this is not an invariable phenomenon One of the conditions with which a chondroma may be confused is a hydatid cyst, the features on which these authors have relied for distinction between the two are the 'nodular periphery and haphazard calcification or ossification of the pulmonary chondromas',

and the absence of any recognized manifestations of echinococcus disease They lay stress on the nodular appearance in the periphery of the X-ray shadow of chondromata in contradistinction to the smooth outline presented by a hydatid cyst

ANGIOMATA

These new growths are of extreme rarity Whitaker (1947), in a report of two recent examples, was only able to find records of 5 cases in the literature Cleland (1948) has added two further cases to the list, and yet another was reported by Boerema and Brilman (1948) of a boy on whom they operated with success

Capillary and cavernous angiomata were included by the late Professor Kettle as varieties of the vascular endotheliomata (cf Chap X), as were also the cavernous lymphangiomata, of which occasional examples have been found in the mediastinum Haemangioma of the lung appears to be associated with a generalized tendency to vascular mal-development, presumably congenital There is some evidence that the condition may be a familial peculiarity Goldman reports an example of haemangioma occurring in each of two brothers

The dilated vessels found in these pulmonary growths vary in size, they may in portions of the lung appear as large lobulated cavities There may be associated haemangiomata in other viscera, e g liver, &c , and telangiectases of the skin and mucous membranes are not infrequently a concomitant feature

In most of the cases reported the angiomata have originated in the lung Adams and Bloch record one instance of haemangioma of the mediastinum The tumour in this case weighed 527 gm and measured 18 by 10 by 5 cm It was successfully removed, and the patient after passing through a very critical and anxious period eventually left hospital 6½ weeks after operation Winklebaum records a case of a malignant haemangioma of the mediastinum This patient died 2 months after operation, and autopsy revealed traces of a primary growth as well as secondary metastatic lesions in the lungs

Clinically the condition may be manifested by attacks of haemoptysis, and in most of the cases recorded this has been associated with polycythaemia, cyanosis, and clubbing of the fingers It is the combination of such a clinical picture with the presence of irregular adventitious opacities in the radiogram that may lead to a diagnosis of the condition, with the possible corollary of removal of the affected lung, which, of course, constitutes the only radical treatment

XANTHOMATA

One of the rarer intrathoracic tumours, specially deserving of mention here owing to its resemblance radiologically to the other varieties already described, is the xanthoma Ewing in his chapter on the fibromata includes the xanthoma or xanthelasma, which he mentions as a yellowish-brown tumour of the skin, seen most often in the eyelids, but occurring also in other regions including the respiratory system

Histologically these growths are conspicuous for their abundance of lipoid globules, associated with large swollen polyhedral cells and smaller spindle-shaped cells The globules are thought to be of the nature of a cholesterin fatty acid ester

Tudor Edwards in 1927 reported, in a series of seven operable tumours within the chest, a case of this type, which was then described as a fibro-liposarcoma This case was referred to later in a publication by Phillips who describes two examples of intrathoracic xanthomatous new growths and gives an excellent summary of the literature with numerous illustrations He suggests very reasonably that, although the various names used to describe growths of this histological character commonly include the word sarcoma, they appear nevertheless to be non malignant in the usual sense of the word and therefore the expression sarcoma is a misnomer and should be dropped

There is nothing in the clinical history of these cases to distinguish them from other forms of benign intrathoracic growths and radiologically they seem to be indistinguishable from other fibrous tumours already described The opacities seen in the radiograms are smooth rounded, and well defined with sharp edges Lateral views show them to be situated in most cases in the posterior part of the mediastinum The tumours vary considerably in size and from a pre-operative diagnostic point of view are most likely to be classed with the neuro-fibromata

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VI

CARCINOMA OF THE BRONCHUS

HISTORICAL AND STATISTICAL

HISTORY

IN an earlier work, published in 1930, I made reference to the historical aspects of lung cancer, which, though apparently unknown to the earliest authors of the Science and Art of Medicine, yet found their way into the literature of the seventeenth century According to Adler, whose well-known text-book on this subject must still rank as a classic, the first publication of results of autopsies on lungs which were probably the seat of cancer was due to Morgagni (1682–1772) The latter has recorded a remarkable description of the case of a man aged about 60 who suffered from a blood-stained purulent expectoration post-mortem examination in this case revealed a lung extremely hard, adherent to the pleura and mediastinum, and the seat of a cancerous ulcer Adler in his comments on this case has suggested that it was in all probability an example of primary malignant growth in the lung That Morgagni had seen the condition with which we are now familiar is probable from the following extracts from an old translation of his original work Referring to some observations on dropsy of the pericardium he says ' . in the second observation there was a scirrhous glandular body which, when the sternum was removed, appeared to be fixed by one extremity to the inferior lobule of the right lobe of the lung and by the other to the mediastinum and diaphragm' Later on he observes 'the dropsy of the pericardium was joined with a dropsy of the thorax, and there were complaints of a great load lying upon the breast, heaviness of the chest, an oppressive pain at the bottom of the sternum, strictures of the chest, anxieties and tightness of the precordia and of the heart being pressed in as it were upon itself' To chest physicians of the present day, well acquainted with the clinical phenomena of bronchial carcinoma in its advanced stages, the foregoing description will doubtless present a familiar picture Another interesting and instructive account is given by Huguenin, who quotes the observations of Boerhave on the post-mortem examination of the body of the Marquis of St Auban, whose death appears to have been due to the pressure of a large pleural effusion The primary cause of this was evidently a pulmonary or bronchial new growth, the exact nature of which does not seem to have been recognized, though Corvisant, who records the case, apparently had in mind the possibility of its malignancy, since he remarks '*je ne sache pas qu'on ait jamais observé un des*

organes pulmonaires dans un etat strictement squirrheux ou degeneré en cancer' Bayle in his studies of pulmonary tuberculosis appears to have included cases in which malignant disease in the lung co-existed with the inflammatory lesions, but according to Huguenin the separation of the two conditions and the recognition of encephaloid cancer of the lung as a pathological entity were due to Laennec

INCIDENCE OF PRIMARY LUNG CANCER

In my original monograph attention was called to an increase in the figures for respiratory cancer, following the First World War, so remarkable that it seemed difficult to suppose that the rise in the frequency of the disease was merely apparent and not real The vivid impression of an influx of cases of pulmonary new growth gained from personal experience in the out-patient clinics of the Brompton Hospital had led to a survey of the literature of the subject available in various countries From this it appeared that the per centage of respiratory cancer in relation both to total cancer and also to total autopsies had shown a steady increase from the latter part of the nineteenth century up to the year 1925 or thereabouts To suggestions that this was explicable by our improved methods of diagnosis the reply was given that the alleged increase in the incidence of primary lung cancer was based not upon clinical records but upon actual post-mortem evidence, and that, since it could hardly be argued that the morbid anatomists of the earlier period were less accurate in their descriptions and diagnoses than those of the present generation, this explanation appeared, to say the least of it, to lose much of its force

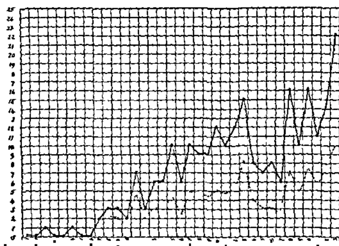
It is hardly necessary to reproduce here all the statistical tables which were quoted at that time and which can easily be traced from the bibliography given at the end of this chapter a brief reference, however, may be made to some of the more important details, which are still widely quoted The most striking, perhaps, of all the graphs of the German figures is Kikuth's curve (Table VI) showing the incidence of bronchial carcinoma based on a survey of 246 cases which came to autopsy in the Eppendorf Hospital, Hamburg over a period of 35 years (1889 to 1923)

of the most important continental centres.

From the United States one of the most interesting contributions was a paper by Barron giving his own record from the Department of Pathology in the University of Minnesota From 1899 to the middle of 1921 there were 13 cases of primary lung cancer (i e 0 29 per cent) From 1899 to 1911 there was not a single case of carcinoma of the lung in a series of 1333 autopsies

From 1912 to 1918 inclusive there were 4 cases in a series of 2 026 autopsies (i e 0 2 per cent), and from January 1919 to June 1921 (a period of 2½ years) 9 cases of primary lung cancer were found out of a series of 1003 autopsies (i e 0 9 per cent for this series)

TABLE VI *Curve Illustrating the Incidence of Primary Bronchial Carcinoma at the Eppendorf Hospital, Hamburg* (Kikuth *loc cit*)



Statistics in this country up to the period of which we are speaking were not on the same scale as those on the Continent and in U S A but tended nevertheless towards the same conclusion, viz that there had been a definite rise in the incidence of primary intrathoracic growths This appeared on the face of it reasonably clear from the report of the International Cancer Conference held in London in 1928 (Dunn and White) from which it transpired that the percentage of cases of intrathoracic cancer had increased from 0 94 in the period 1903–7 to 1 69 in the period 1923–7

In spite of the convictions of those constantly working on the clinical side in chest hospitals whose practical experience of lung cancer as an increasingly common phenomenon was in marked contrast to its unquestioned rarity in

their student days, there was at this time no little hesitancy on the part of many in accepting the view that this disease was really on the increase The correct interpretation of statistics is admittedly a special science and many fallacies obvious to the expert are apt to be a constant pitfall to those who have not had special training in this direction Some of these difficulties have been critically discussed by Passey (1935) in a review of the incidence of intra thoracic new growths in the teaching hospitals of Great Britain He there pointed out that, in so far as the autopsies in these hospitals might have been and most probably were to some extent selected, conclusions drawn from the ratio between post-mortem records of lung cancer and the total number of autopsies performed might well be misleading For example, a diminution in the total number of post-mortem examinations performed per annum (and this occurred in many of the large centres during 1914–18), alone might tend to show a rise in the percentage of lung cancer based on total autopsies The Leeds autopsies, it appears, underwent no appreciable diminution during the

TABLE VII *Incidence of Bronchial Carcinoma* (Huguenin, *loc cit*)

Worker	*Period*	*Percentage*
Staehelin (Basel)	Before 1906	1 76
	1906 to 1914	2 9
	1914 to 1924	5 0
Seyfarth (Leipzig)	1900 to 1906	5 01
	1907 to 1913	6 88
	1914 to 1918	11 23
	1919 to 1923	8 75
	First half of 1924	15 5
Dora Hanf (Berlin)	1903 to 1906	3 3
	1922 to 1925	7 5
Wahl (Berlin)	1917 to 1922	6 0
	1922 to 1927	13 0
Kikuth (Hamburg)	1910 to 1914	5 5
	1915 to 1919	4 2
	1920 to 1924	7 7
Probst (Zurich)	1906 to 1910	1 13
	1911 to 1915	3 34
	1916 to 1920	6 12
	1921 to 1925	7 17
	1926	7 56
Zalka	1919 to 1923	2 67
	1924 to 1927	6 65
Berblinger (Jena)	1910 to 1914	2 2
	1915 to 1919	2 9
	1920 to 1924	8 3

First World War, and the figures compiled by Bonser in regard to lung cancer were remarkable in that out of all English statistics they alone failed to show the rise noted by other observers in this country A few years later, however, Bonser reported an increase in the male incidence as compared to the female, and thought that this supported the view that the increase in lung cancer was real

[illegible]

per 100,000 living, and among females from 4 to 7 per 100,000, the sex-ratio changing from about 5 4 to 3 1 These figures for the capital as a whole are compared with those for the Central Tuberculosis Station, where excellent diagnostic facilities have been available for all patients throughout the period It is shown that only a slight increase and no steady rise has been noted in this clinic from 1936 to 1945, and that the sex-ratio is 8 1 They conclude that the increase in reported lung cancer mortality is chiefly due to improved diagnosis and may be expected to continue until the sex-ratio reaches 8 1 It would be surprising if the diagnosis of bronchial carcinoma had not materially improved, and some of the reported increase may well be due to this cause, but even the figures quoted for the Copenhagen Tuberculosis Station show an increase which, for some age groups at least, is significant and considerable If the increase in mortality recorded is all due to diagnosis, then several thousand patients who died of this disease each year before, were recorded under a false diagnosis, and some decrease has occurred which balances the new lung cancer mortality There is no corresponding decrease to be found among the possible false diagnoses of malignant disease, though it must be adm tted that the nu mber of deaths attributed to infect [illegible]

[illegible] 1940–4 at ages 45 to 65, and that the mortality from lobar pneumonia, for instance, which is decreasing is considerably greater among men than among women

I have mentioned these points for the sake of completeness and in order that those of my readers who may be specially interested in the statistical aspects of this subject may not have cause to complain that all relevant views on the matter have not been fairly represented Some of the details given in the earlier part of this chapter were the subject of a good deal of controversy at a time when there was no question in the minds of the pioneers of thoracic surgery that primary bronchial carcinoma was becoming a distressingly common clinical problem not only in hospital but also in private practice, and that, whatever the disease might have been in the past it was by no

TABLES IX AND X *Cancer of the Lung and Pleura Death rate by Age groups*

TABLE IX

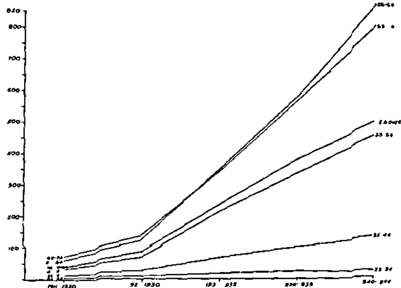


TABLE X

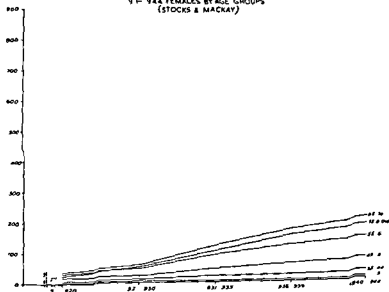


TABLE XI *Incidence of Bronchial Carcinoma and of Laryngeal Carcinoma* (Kennaway and Kennaway)

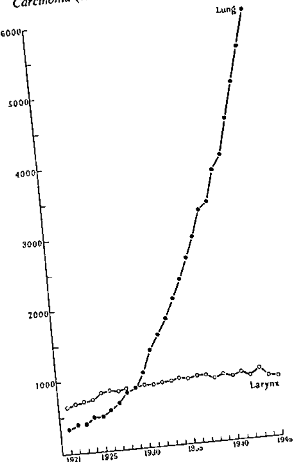
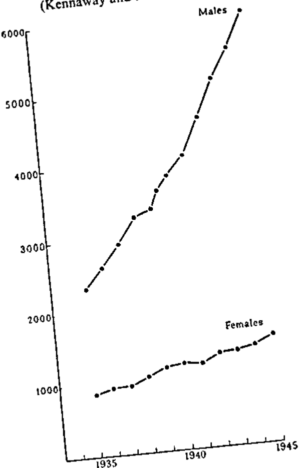


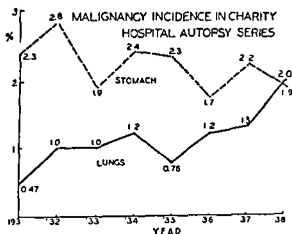
TABLE XII *Sex Incidence of Bronchial Carcinoma* (Kennaway and Kennaway)



cancer 47 per cent had post-mortem examinations, the clinical diagnoses before death being as follows certain, 37 per cent, uncertain, 26 per cent, unknown, 15 per cent, and not stated, 22 per cent

Comparison has already been made between the incidence of carcinoma of the bronchus and that of carcinoma of the larynx It is also of interest to note the relative incidence of gastric and lung cancer in autopsies performed at the Charity Hospital over an eight-year period This is illustrated in Table XIII from a paper published by Oschner and De Bakey (loc cit)

TABLE XIII *Incidence of Lung Cancer Compared with that of Gastric Cancer* (Oschner and De Bakey)



The number of cases which in the last few years have appeared in the out patient departments and wards of the big London hospitals, urgently demanding priority in view of the increasing possibilities of successful surgical treatment is truly appalling While admitting the difficulty of the correct interpretation of statistics and the numerous possible fallacies incidental to their study, I cannot but feel that some of the most recent figures quoted can hardly fail to corroborate the opinion prevalent among chest specialists that cancer of the lung, which in the nineteenth century was an acknowledged rarity, even in the post-mortem room, has now become an extremely common disease

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VII

CARCINOMA OF THE BRONCHUS

PATHOLOGY AND AETIOLOGY

HISTOLOGY

THE proper histological differentiation of primary malignant growths of the respiratory tract is a matter of no little difficulty in the last few years a vast amount of literature has appeared on the subject, on which there are still some differences of opinion among various authors The microscopic appearances in individual lung cancers may vary considerably, the tendency to metaplasia being, perhaps, somewhat greater than in similar growths found elsewhere in the body Although numerous types of cell may be seen in any one tumour, it is usual to classify these growths according to their main structural characteristics, and most authorities are now agreed in recognizing three chief groups, the anaplastic carcinomata, the adeno carcinomata, and the squamous carcinomata, in each of which one type of cell is generally predominant

The anaplastic (ἀναπλάσσειν—to form anew, to remodel) growths include in all probability those which were formerly described in Adler's original monograph as lymphosarcomata of the mediastinum and which were later designated by Barnard 'oat-celled carcinomata'. Their cells are for the most part oval or spindle shaped, with relatively large, deeply staining nuclei and little cytoplasm, though cuboidal, columnar, or squamous types of cell may also be seen in the same tumour mass In the adeno carcinomata the cells are mostly spheroidal or columnar, but other forms may also be seen The squamous-celled growths are similar to the epitheliomata found in other parts of the body, the cells being mostly of the large polygonal variety, with paler staining nuclei and relatively more cytoplasm than in the oat-celled type of tumours prickle-cells may be seen, and sometimes there is evidence of keratinization (See Figs 50 to 53)

The anaplastic growths would seem to be on the whole the commonest among the primary lung cancers In Barnard s original paper only 7 out of the 19 malignant tumours of the lung and mediastinum discussed were obvious carcinomata Of 68 cases examined by Duguid 32 (i e 47 per cent) were described as being of the oat-celled variety, the remainder including the large celled alveolar type and the squamous carcinoma Willis, in a recent histological review of 84 autopsy cases, gives the following analysis of his findings in different parts of the growths, primary and secondary



FIG 50 Microphotograph (×130) of squamous-cell carcinoma of bronchus (From the Pathological Department of the Royal Cancer Hospital by courtesy of Prof R A Willis

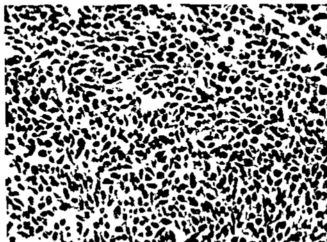


FIG 51 Microphotograph (×450) of anaplastic oat-cell carcinoma of bronchus (From the Pathological Department of the Royal Cancer Hospital by courtesy of Prof R A Willis

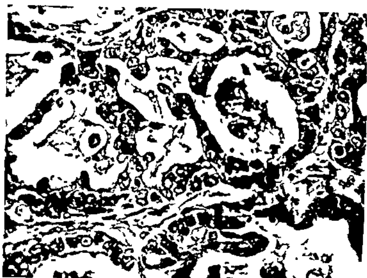


FIG 52 Microphotograph (×300) of adeno-carcinoma of bronchus (From the Pathological Department of the Royal Cancer Hospital by courtesy of Prof R A Willis)

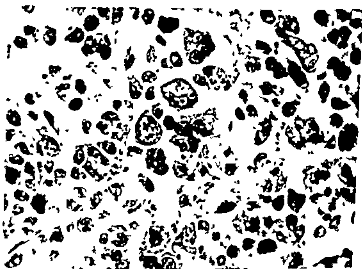


FIG 53 Microphotograph (×450) of anaplastic pleomorphic-cell carcinoma of bronchus (From the Pathological Department of the Royal Cancer Hospital by courtesy of Prof R A Willis)

TABLE XIV *Types of Growth in Bronchial Carcinoma* (Willis)

Type of growth	*Number*	*Per cent*
Anaplastic carcinoma only including oat celled spindle celled spheroidal celled and pleomorphic-celled	37	44
Adeno-carcinoma only including acinar papillary mucoid and signet ring structure	16	19
Squamous carcinoma only	12	14 3
Combined anaplastic and adeno carcinoma	8	9 5
Combined anaplastic and squamous carcinoma	5	6
Combined anaplastic squamous and adeno-carcinoma	4	4 76
Combined squamous and adeno carcinoma	2	2 38
Total	*84*	99 94

Origin There was at one time a certain amount of dispute about the actual site from which these tumours originated and some authorities maintained that the growth of cancer from alveolar epithelium though not proven was at any rate a possibility This view is no longer entertained and it is now generally accepted that all so called primary lung cancer is in reality bronchial cancer the growth of whatever type having its origin in the bronchial epithelium or in the deeper glands of the bronchial submucosa In those cases in which the main tumour mass appears to be situated within the substance of the lung itself without obvious involvement of the main bronchi or of their larger branches it is presumed that the growth has started in one of the smaller peripheral bronchial divisions and has thence spread gradually into the lung parenchyma Growths thus peripherally situated do not as Willis has pointed out differ either in their histological structure or in their general behaviour from those whose origin from a bronchus is obvious there no longer appears any adequate evidence or reason to suppose that any primary lung cancer originates from the pulmonary alveoli

Gross Morbid Anatomy From the clinician s point of view the histological classification of lung cancer possesses but a limited importance It may be said perhaps that on the whole the outlook for surgery in squamous carcinoma of the bronchus is somewhat more favourable than is the case with growths of the anaplastic type in so far as the former seem to be slower growing tumours with less tendency to early and widespread metastasis This however is a very general statement and in practice there will be found numerous disappointing exceptions The study of the naked eye morbid anatomy of this disease does materially help our understanding of its symptomatology of the development of the clinical picture and of some of the difficulties that may be presented both in the clinical and in the radiological examination of these patients

In a large proportion of cases the growth has a more or less typical site of origin a few centimetres below the division of a main bronchus at the point

where the smaller bronchi take off At autopsy the main portion of the growth is found as a nodular mass situated at the hilum whence it may be seen spreading out fanwise toward the periphery Thick, continuous, whitish cords may be seen radiating from the hilum into the lung substance and following the divisions and sub-divisions of the bronchus down to the smallest branches Sometimes a large portion or even the whole of the lung may be entirely replaced by growth, which appears as a solid mass of white or yellowish-white material encircling and obstructing the bronchus (Fig 54) Occasionally a main bronchus is completely occluded, and growth can be seen spreading over the carina into the lumen of the opposite bronchus The main mass may on the other hand be confined to one lobe (very often the right upper lobe), being more or less sharply delimited by the interlobar septum Some growths are found almost entirely within the lumen, with little evidence of external spread beyond the bronchial wall, though large masses of malignant lymph nodes may be present in the posterior mediastinum In some instances a spread of the growth occurs along the bronchial wall involving the bronchial tree for a considerable distance, even down to the smallest peripheral divisions, without any appreciable encroachment upon the surrounding lung parenchyma (cf Fig 55) The peripheral tumours, which originate in the mucosa of one of the smaller bronchial divisions, are seen as round or oval masses, more or less circumscribed, within the substance of the lung occasionally occupying the greater part of a lobe, but not involving the hilum Sometimes the actual primary mass in the bronchus may be very small, its true nature being determined only by subsequent microscopic examination, *though metastases in the regional lymph-nodes and elsewhere may have* already occurred

When the lung tissue has been extensively invaded, the growth is often found to be soft in the centre and the whole mass may contain irregular cavities with coarsely granular walls continuous with those of the bronchus Such cavities are usually filled with pus in which may be found broken down lung tissue and portions of growth Where the main mass is confined to the hilum there is often a considerable degree of bronchial stenosis due to extrinsic pressure by the tumour, and in such circumstances there may be bronchiectatic changes in the corresponding *lung area distal to the obstruction* Not infrequently the primary bronchial growth is relatively small and the main mass, consisting of secondarily affected lymph nodes may be found in the mediastinum, in some cases infiltrating the pericardium and roots of the great vessels, or even penetrating into the auricles of the heart, in which it appears in the form of nodules in the interior

Some of the main features of the gross morbid anatomy may be seen in the accompanying illustrations, Figs 54-6

Site of Growth. The general experience of most observers has been that the right lung is affected more often than the left, and the upper lobe rather more than the lower lobe, but there is no very constant or striking difference in

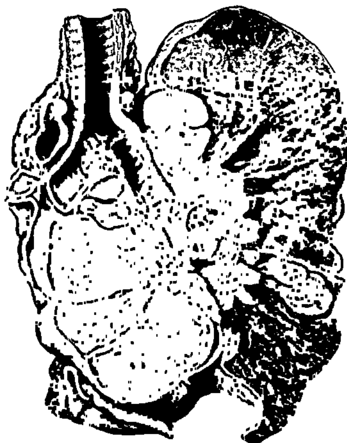
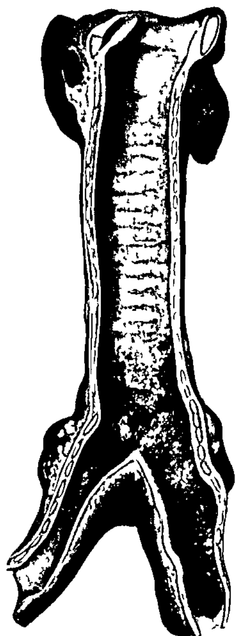


FIG 54 Macroscopic appearances in primary lung cancer The main bronchus is completely occluded by the growth which has spread out into the substance of the lung (Drawing of specimen in the Brompton Hospital Museum) (From Davidson's *Practical Manual of Diseases of the Chest*)

either of these respects In Simpson's series of 139 cases the right and left lungs were involved with equal frequency (right, 69, left, 70) The upper lobe was affected more often than the lower (upper, 41, lower, 29, indeterminate, 67) In my own series of 107 cases at Brompton the right lung was affected in 59 and the left lung in 36 In 12 cases the growth was more or less centrally placed, chiefly in the mediastinal region and not involving one side more than



[illegible] appearances in primary

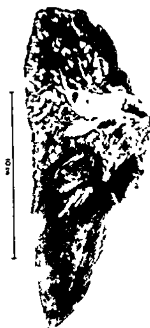


FIG 56 Macroscopic appearances in primary bronchial carcinoma (Photograph of specimen in the Brompton Hospital Museum)

the other Kikuth (1925) gave the following distribution right upper and middle lobes, 38; right lower lobe, 35, left upper lobe, 31, left lower lobe, 30 More recent figures are given by Willis whose 84 cases were distributed as follows right lung, 45, left lung, 36, at the bifurcation, 2, diffusely, 1 He quotes Simon's 2,177 cases right lung, 1,147, left lung, 992, both lungs, 38, the lobar distribution of 649 tumours being right upper lobe, 169, right middle lobe, 70, right lower lobe, 119, left upper lobe, 179, and left lower lobe, 112

Metastasis. More important by far than the site of the primary tumour is its behaviour especially with regard to its rate of growth and its tendency to dissemination by metastasis The frequency and the widespread distribution of metastatic deposits from bronchial carcinoma are recognized by all writers who have published series of cases, and there is general agreement as to the relative frequency with which distant regions are involved Apart from the regional lymph nodes, the liver appears to be the commonest site after the liver come the lungs themselves the bones, the brain, the kidneys and suprarenals, the pancreas, the heart and pericardium, the thyroid, colon, stomach and spleen, the gall bladder, and the ovaries The lymphatic glands are almost always affected at a fairly early stage In Simpson's series the hilar or mediastinal glands were involved in 104 out of 139 (75 per cent) and in Willis's series in 76 out of 84 (90 per cent) In some cases, as we have already observed, the main mass seen at autopsy is formed by the posterior mediastinal lymph nodes which are infiltrated with carcinoma, the original bronchial tumour being still relatively small This is a common finding with growths of the oat-cell type, which tend to metastasize early and widely in comparison, for example, with the squamous carcinomata If, as sometimes happens, a primary growth near the root of the lungs spreads by direct extension into the mediastinum, it may be a matter of some difficulty at first out of a large mass which has involved the pericardium and main blood-vessels to distinguish the regional lymph-nodes from the primary mass itself The tumour may spread to the supraclavicular glands, occasionally to the [illegible]
[illegible]
[illegible]
during life, even before obvious clinical evidence of intrathoracic disease) The central nervous system is also a frequent site of secondary deposits which may be the first source of manifest symptoms (cf Chap VIII, p 94) The pleura may be the site of multiple secondary nodules or it may be involved by direct extension of the primary growth The bones are often affected, here again this is sometimes the first cause of symptoms during life and may be a source of distressing errors in diagnosis

Of the rate of growth and general course of bronchial carcinomata it is

difficult to speak with precision, so great is the variation in these respects of the behaviour of individual tumours Some are relatively slow, others rapid in their growth Some give rise to early and widespread metastases (this seems to be more especially the case with oat-celled tumours), others do not It is, of course, impossible to be dogmatic on the point, but the squamous carcinomata, as we have already remarked, do appear to be somewhat less rapid in their growth and less likely to disseminate early, and for this reason are usually regarded as somewhat less unfavourable from the therapeutic standpoint Rienhoff in an analysis of 181 consecutive cases of primary lung cancer in which operation was performed gives figures which tend to support this view His cases are divided histologically into two main groups, (*a*) the squamous carcinomata and the 'flat cell' carcinomata, and (*b*) the adeno-carcinomata, with which were included the cylindrical-celled and oat-celled types The first of these groups comprised 64 per cent of the cases in this series and the survival rates based on the histological characters of the growths showed that the squamous and flat-celled types lived a greater length of time than the others The experience of most thoracic surgeons would appear to be similar

Judging from various statistical tables the expectation of life in bronchial carcinoma from the time of the appearance of symptoms is approximately a year at most, the average being nearer 6 months This, of course, gives no indication as to the rate of growth of the tumour since we have no data which enable us to estimate how long it has been in existence before it has given rise to symptoms There is reason to think that in some instances it has lain dormant in the body for a considerable period of time Willis (1938) reported one case in which a small and unsuspected growth was thought to have been in existence for 8½ years it was discovered at autopsy

AETIOLOGY

The aetiology of primary lung cancer has been and still is the subject of much speculation Apart from the conventional consideration of figures relating to age and sex-incidence and of questions of heredity, trauma, occupation, and so forth, which bulk largely in the discussion of most cancer problems, the prevalence of respiratory carcinoma has led to the advancement of numerous hypotheses, chiefly concerned with supposed sources of irritation of the respiratory tract, in order to account for it

The details regarding age and sex incidence are not in dispute All reliable figures show an undoubted preponderance of males over females, and the average age appears to be round about 50 The following tables may be taken as representative

TABLE XV *Age incidence of Primary Lung Cancer in 173 cases* (Duguid)

No of cases	Age-period	Per cent	No of cases	Age-period	Per cent
5	under 21	2 9	33	46–50	19 0
9	21–5	5 2	25	51–5	14 45
6	26–30	3 5	25	56–60	14 45
11	31–5	6 36	5	61–5	2 9
20	36–40	11 55	6	66–70	3 5
27	41–5	15 6	1	71 5	0 58

TABLE XVI *Age incidence of Primary Lung Cancer in 107 cases* (Davidson)

No of cases	Age-period	Per cent	No of cases	Age-period	Per cent
2	under 21	1 87	20	46–50	18 7
2	21 5	1 87	14	51 5	13 0
4	26–30	3 74	16	56–60	15 0
11	31–5	10 28	5	61 5	4 67
9	36–40	8 41	0	66–70	0
21	41–5	19 62	1	71 5	0 93
	2 cases were aged 75–80 = 1 87%				

Willis observes that lung cancer affects rather younger people than most other varieties of carcinoma he gives the following figures for his series of 84 autopsy cases

TABLE XVII *Age-incidence of Primary Lung Cancer in 84 cases* (Willis)

Decade	3rd	4th	5th	6th	7th	8th	9th	Total
No of cases	1	5	15	31	22	9	1	84
Per cent	1	6	18	37	26	11	1	100

The condition is rarely found in the very young but a few examples are recorded in the literature Hauser, reviewing the literature mentions three instances of primary lung cancer in infancy, one a boy of 5½ months (McAldowie), one a girl of 16 months (Schwyter), and a third in a female infant aged 16 months (Beardsley) he adds a case of his own, a carcinoma of the left lung in an infant of 17 months

Primary lung cancer in a girl of 9 years is recorded by Dick and Miller, another case in a girl of 4 years and 4 months is given by Field and Quilliam The table on p 86 (Table XVIII) of cases under 21 years of age collected from the literature by Hauser, is among the most recent records

The various statistics show little material variation in regard to sex incidence Seyfarth gives the male–female ratio as 5 73 to 1 (303 cases), Probst 4 43 to 1 (76 cases) Katz 3 to 1 (56 cases) and in this country, Duguid 6 3 to 1 (175 cases), Simpson 4 to 1 (139 cases), Brompton Hospital (Davidson) 5 to 1 (107 cases), Willis 5 to 1 (84 cases)

TABLE XVIII *Cancer of Lung in Childhood and Early Adult Life* (Hauser)

Author	*Year*	*Age*	*Sex*	*Histology*
Werner	1891	19	F	Carcinoma
Horn	1907	18	F	Adeno-carcinoma
Hirsch and Ryerson	1928	5	M	Carcinoma
Simpson	1929	13	M	Carcinoma
Kilduffe and Salasin	1933	14	M	Carcinoma
Gould	1934	10	M	Carcinoma
Cathala and Ducas	1935	10	M	Malignant embryonal tumour
Lerebullet Garnier and Courtial	1935	5	F	Carcinoma (small-cell)
Cardelle et al	1936	11	M	Carcinoma (small-cell)
Adamson Boyd and Cameron	1936	19	M	Anaplastic carcinoma

General Considerations The literature of the last 25 years reveals an exhaustive study of the various factors that have been supposed, rightly or wrongly, to have some bearing upon the development of cancer of the lung in man A word may be said here on the alleged importance of previous respiratory infections, e g pneumonia, bronchitis, influenza, &c, on which in earlier commentaries no little stress was laid Much of the force of the arguments adduced in favour of the aetiological importance of these diseases was lost when the significance of pulmonary collapse in bronchial carcinoma was more fully realized There is no doubt that attacks of so-called pneumonia or influenza which appear in many of the clinical histories, are in reality phenomena associated with lobar or segmental collapse, with accompanying infection, following obstruction of a bronchus by a primary growth

The association between tuberculosis and lung cancer has been noted in a few instances it is true that the two conditions may coexist but the proportion in which tubercle is found is very small and there seems no real ground for supposing that there is any causal connexion between the two conditions Heredity, trauma, and other general factors have been discussed, but no evidence has been forthcoming to indicate that these have any special significance

In recent literature the two factors which have received most attention are occupation, and the possible effects of chronic irritants on the respiratory tract An enormous amount of work has been done on the classification of the occupations of persons dying from respiratory cancer Kennaway and Kennaway investigated the details over the period 1921–32, and in a later paper they dealt with further figures for the succeeding 6 years and presented the data for the whole 18-year period 1921–38 The occupations examined numbered 63, and embraced about 30 per cent of the male population of 20 years of age and upwards The details of these papers are exhaustive and deserve the most careful study, but the authors are unable to reach any conclusion that would justify some of the notions that have been popularly entertained regarding the

relation between lung cancer and occupational or environmental factors One of their conclusions may be quoted by way of example

> A group of open air occupations where there is exposure to the dust of roads has rat os above 100 for cancer of the lung and of the larynx with the exception that motor drivers have a normal liability to cancer of the larynx But the comparative incidence of cancer of the lung is not increasing distinctly in any of these occupat ons and in the paviours street masons concretors and asphalters there has been a distinct fall in the rat o

The possible effects of inhalation of tar fumes of petrol &c have long constituted a favourite topic for argument Kennaway and Kennaway in their last report note a tendency to increased prevalence of lung cancer in workers exposed to coal gas and tar but say that in the later period studied the incidence was not found to exceed two and a half times that of the general population They further remark— experimental pathology has not yielded any conclusive evidence on this question (possible causes of cancer of the lung in man) as it has done in the case of the occupational cancers of the skin Most of the laboratory work such as that of Argyll Campbell has been done on the mouse in which species the neoplastic factors in the lung are certainly different from those in man

The frequency of lung cancer among the workers in the Schneeberg mining districts in Saxony has been recognized for many years and reference is made to this by practically all writers on this subject A very full communication by Rostoski and his colleagues in 1926 showed that pneumonokoniosis was common in these workers X ray examination revealing two main groups (*a*) pure pneumonokoniosis and (*b*) pneumonokoniosis with shadows suggestive of neoplasm Out of 154 cases investigated 21 died during 3½ years observa tion and in 13 of these (i e 62 per cent) carcinoma was found at autopsy The Schneeberg dust contains metallic sulphides of iron and arsenides of cobalt and nickel together with much quartz other stony constituents and particles of steel from the tools It is also noted that the radium content is unusually high A very high incidence of carcinoma of the lung is also seen among the workers in the radium mines of Jochymov in Czechoslovakia The general conclusion by the most recent workers is that of all these possible carci nogenic substances radon is probably the most important

In the above paragraphs I have attempted no more than the most general outline of the work that has been done on the environmental factors which may be concerned in the development of respiratory cancer for the details of which readers must be referred to the various original publications mentioned in the bibliography It still remains true that the cause of bronchial carcinoma is unknown and that no adequate scientific evidence so far is available to enable us to associate it with any known specific causative or aggravating

Sir William Gull a few years later gives an account of a man of 61 admitted to Guy's Hospital, emaciated and cachectic, who had been ill for 4 months with pain in the right side but without cough On examination the right side of the chest was completely dull on percussion, the whole side being flattened and the infraclavicular space depressed On auscultation no respiratory murmur was audible at any part on this side, nor could any tactile vibration or vocal resonance be detected At the post-mortem examination of this patient the pleura was found to be universally adherent, and there was fibrous thickening and induration (? malignant) *around the bronchus*, involving the trunk of the right vagus and the branches of the pulmonary plexus The pulmonary tissue was consolidated into a state of grey and iron grey hepatization, and in the lower part of the upper lobe was a large sloughing cavity from the breaking up of the indurated tissue The left lung was healthy In his commentary on this case Gull notes that the diminution in the whole volume of the lung, as shown by the flattening of the chest and falling in of the infraclavicular space, was probably caused by the collapse of the tissue which followed upon paralysis of the bronchi [*sic*] He concludes as follows

> 'The chief point worthy of note in the physical diagnosis is that when the paralysed bronchi become choked the respiration in the part is greatly enfeebled, if not altogether absent and hence there are no indications from the entrance of the air of the state of the pulmonary tissue There may be dullness on percussion, absence of vocal resonance and respiratory murmur and immobility of the chest not because there is effusion of fluid or some cancerous or other growth but because the bronchi are obstructed and immobile and the tissue of the lung consolidated '

The above are taken from among some of the famous descriptions by well-known clinicians of the condition with which we are familiar at the present day, but which to them was undoubtedly a rarity The following case of advanced cancer of the lung remarkable for the somewhat unusual duration of the manifest symptoms, may be cited as an example of a clinical picture which is not uncommon

A man aged 47 was seen in the out-patient department at Brompton in June 1922 with a history of pain in the chest and cough dating approximately from an attack of so-called influenza with pleurisy in the previous February On examination of the chest the whole of the left side in front and behind was dull on percussion, except at the apex Breath-sounds, vocal resonance, and tactile fremitus were practically absent The heart was displaced, being drawn completely over to the left side He was admitted with a diagnosis of 'fibrosis of the lung and old pleurisy' X-ray examination showed a general diffuse opacity of the whole of the left side of the chest After 8 weeks in hospital his general condition seemed much improved and in October he was transferred to a convalescent home On his return to London a month later

he had a sudden fit of coughing and brought up about half a pint of yellowish fluid containing streaks of blood When he was examined again in the out-patient department shortly after this, the extent of dullness on the left side of the chest seemed appreciably less, and re examination by X-rays showed that the opacity previously noted had cleared considerably It was thought that he must have had either an interlobar empyema or a localized pulmonary abscess that had ruptured into a bronchus, and after a surgical consultation it was decided that, since there had apparently been adequate drainage, no further intervention was indicated at the moment This patient continued to attend at intervals and kept in comparatively good health until March 1924, when he again had a sudden fit of coughing and brought up about an egg-cupful of pus He was readmitted for investigation the chest was explored with a needle on two occasions without result About this time he had begun to suffer from severe dyspnoea which frequently came on in sudden paroxysmal attacks There was some irregular pyrexia (97 4 to 100) A blood count on April 4th showed the following picture

Red cells	3 200 000
Haemoglobin	90%
Colour index	1 4
Total white cells	15 000
Differential count	
Polymorphonuclears	64 3%
Small lymphocytes	22 7%
Large lymphocytes	9 3%
Eosinophiles	3 3%
Basophiles	0 4%

The chest was explored again with a needle on April 12th, but only a small bead of pus was obtained which yielded no growth on agar culture No tubercle bacilli were found Examination of stained films showed numerous pus cells, no giant cells were seen In view of the leucocytosis and the pyrexia, as well as the previous history of expectoration of pus, it was decided to explore the chest under a general anaesthetic This was done, an aspirating needle being put into the chest posteriorly at the level of the 5th interspace Purulent fluid was found A portion of the 5th rib was resected, the exploring needle being left *in situ* The parietal pleura being free, contrary to expectation the wound was packed with gauze and the patient was returned to the ward About a week later the wound was re opened and the pleura incised and the lung explored at the site at which the pus had been aspirated No more pus was found after repeated exploration in various directions Two days later during the dressing of the wound a considerable discharge of thick pus occurred

The discharge continued in gradually decreasing amount and by May 18th the wound appeared to be healing On May 26th he had a sudden attack of pain in the right lumbar region, and also complained of dyspnoea From this time onwards paroxysmal attacks of dyspnoea occurred with increasing frequency and were often brought on by the slightest exertion On June 19th, 1924 he had an unusually severe attack and after a quarter of an hour of great respiratory distress he collapsed and died

At autopsy an extensive carcinomatous growth was found involving the whole of the left lung, completely occluding the left main bronchus, and spreading over the bifurcation of the trachea into the right bronchus The glands in the posterior mediastinum were infiltrated with growth The main mass of growth in the lung was cheesy and was breaking down It extended into the pericardium and involved the ventricular muscle to some extent

I have quoted in some detail the notes of the above case in order to give the reader one representative picture of lung cancer as it appeared nearly 30 years ago, at a time when a fresh interest in the subject had been awakened by the unusual number of cases that were beginning to make their appearance with alarming regularity Practically all the cases diagnosed at that period were in a fairly advanced stage of the disease and would have been found inoperable had they been subjected to exploratory thoracotomy In view of the fact that in practice today a very large proportion of the patients who consult a specialist for this condition fall into a similar category, it may be useful at this point to recapitulate the general clinical and radiological features which then formed the basis of diagnosis and on which the practitioner still has to rely in a large number if not in most of the cases that come to his notice

History and Mode of Onset. Occasionally one still sees patients in whom an intrathoracic cancer has advanced to such a point as to cause gross pressure effects, but who have not sought medical advice until the corresponding respiratory embarrassment has become really distressing In others the clinical history and physical examination suggest the pressure within the chest of some localized suppuration, e g an empyema or a lung abscess (cf the case quoted above) Not uncommonly the first indication of anything amiss is the onset of a pleural effusion A number of patients seek advice primarily on account of sudden haemoptysis, usually slight, the cause of which has either not been determined or has erroneously been thought to be tuberculosis of the lung In a great many instances the onset of illness is slow and insidious, in fact this group of patients, who often present no gross clinical evidence of serious structural disease in the chest, forms perhaps the majority of the cases of bronchial carcinoma which escape detection in the earlier stages

This rough practical classification of lung cancer into the five main groups

above indicated will serve to simplify the problem to some extent from the practitioner's point of view, and since, as we have said, the majority of cases that he sees are likely to fall under one of these five headings, I have thought it useful to retain it Before discussing in detail the symptomatology and physical signs, I would make some further brief general observations on each of these five groups

1 The picture of a patient with obvious and advanced intrathoracic cancer is reminiscent of some of the descriptions given in the older text-books of general medicine in the days when primary malignant lesions of the lungs or bronchus were an acknowledged rarity, and post-mortem specimens of the condition were, even in the largest pathological museums, few and far between Nevertheless, cases are still occasionally encountered in practice Respiratory distress is often extreme, the patient may be cyanosed, evidence of pressure on the superior vena cava is seen in the presence of large, distended, superficial veins on the anterior surface of the chest, with oedema of the upper limbs and even of the chest wall Immobility of one side of the chest with stony dullness on percussion and complete absence of breath-sounds, vocal resonance, and tactile vocal fremitus indicate the replacement of the normal spongy lung tissue by a solid mass In addition there may be large hard lymph nodes in the supraclavicular fossae and/or in the axillae, and irregular enlargement of the liver, owing to extensive metastatic spread of growth via the lymphatics The general picture is similar to that in advanced cases of Hodgkin's disease, aortic aneurysm, benign intrathoracic growth, or other conditions in which mechanical pressure on vital structures occurs from any large abnormal mass within the thorax In most instances the patient's distress is obvious, but occasionally, though the physical signs of pressure are unmistakable, he may be relatively free from discomfort and unaware of the gravity of his condition

2 In not a few cases of intrathoracic suppuration the underlying cause of the trouble is not immediately obvious and in such circumstances the possibility of a malignant neoplasm must always be borne in mind, especially in middle-aged or elderly patients The case-report which I have already quoted gives an example of this Some of the slow growing bronchial carcinomata give rise to no symptoms until the growth begins to break down when cough, pyrexia, and the appearance of an abnormal intrapulmonary opacity in the radiogram combine to give a picture suggestive of an inflammatory lesion in the lung A diagnosis of lung abscess may be made, correct indeed so far as it goes, for the abscess may in fact be present, but incomplete since it fails to indicate the true underlying cause which, even if it has been suspected at first, may not perhaps be demonstrated until it is disclosed by an exploratory operation, or even until necropsy

3 Pleural effusion is sometimes the first indication of a growth of the lung

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examination has shown that death was due to the deposit in the brain of metastatic tumours originating from a primary malignant growth in the bronchus which had caused no manifest respiratory disturbance during life Wyburn *Mason has recorded 3 cases of bronchial carcinoma presenting as* a polyneuritis, the pulmonary symptoms being completely in abeyance, the patients having come for advice solely on account of their neuritic pains

Ellman and others have noted cases of gross pulmonary osteo-arthropathy associated with lung cancer in which the lung tumours were practically symptomless In one at least of Ellman s cases the joint condition improved rapidly after a successful lobectomy, and 2 years later the joint and soft tissue swellings had almost completely subsided The diagnosis of bronchial carcinoma was substantiated after the lobectomy by histological examination of the tumour

Symptomatology. The symptoms of lung cancer vary considerably in individual cases and my experience has led me to the conclusion that despite the various statistical tables of their relative frequency they can only be described in general terms One of the best summaries is that of Harnett, based on figures supplied by the British Empire Cancer Campaign In a statistical survey of 1 063 consecutive cases he gives the first symptoms, *arranged in order of frequency, as follows*

TABLE XIX *Relative Frequency of Symptoms in Bronchial Carcinoma* (Harnett)

First symptom	*Cases*	*Per cent*
Cough	329	32 1
Pain in Chest	190	18 5
Symptoms of pleurisy or intrathoracic infection	95	9 3
Dyspnoea	92	9 0
General asthenia	90	8 8
Haemoptysis	89	8 7
Symptoms due to metastases	71	6 9
Dysphagia or regurgitation	18	1 8
Hoarseness and other symptoms	15	1 5
Pressure symptoms	12	1 2
Discovered on examination or at autopsy	23	2 2

He notes further that 46 per cent of the patients consulted a doctor within 1 month and 64 per cent within the first 3 months of their initial symptoms In 21 per cent of the cases is was impossible to determine this interval, since the patients had complained of a chronic cough for several years

I am inclined to think that even the most carefully compiled tables of symptoms are apt to be a little misleading since out patients are notoriously vague in their statements and descriptions, which are prone to variation on

in a patient who has not previously complained of anything sufficient to induce him to seek medical advice, though on taking a complete history of the illness one may elicit a story of other symptoms which hitherto he has not thought it worth while to mention As in young adults the commonest cause of a primary pleural effusion is an underlying tuberculosis, so in older patients, e g from 45 to 60 or thereabouts, pleural effusion should always raise the suspicion of primary lung cancer, and if the effusion is found to be uniformly blood-stained, this is almost pathognomonic of malignant disease in the chest

4 Blood-spitting is a common initial symptom, and cases which come under this heading are of special importance since they account for an appreciable proportion of instances of haemoptysis of uncertain origin with which sooner or later every general practitioner is faced and which are frequently attributed to pulmonary tuberculosis, sometimes in the absence of any adequate evidence The age of the patient may be of considerable significance As in young adults the commonest cause of haemoptysis is undoubtedly tuberculosis of the lung, so in older patients it only too often denotes a bronchial carcinoma, and the suspicion of this should not be lessened by the absence of abnormal physical signs or even of pathological adventitious shadows in the radiogram

5 Those patients whose history of respiratory symptoms is long and insidious, and whose malignant lesion has been diagnosed as a simple chronic bronchitis, are among the more difficult problems of diagnosis the practitioner's task being rendered none the easier by the fact that physical signs are often minimal and the symptomatology has little to distinguish it from that of the ordinary bronchitic who represents such a large proportion of the doctor's regular clientele

There is one other group to which a brief reference may be made here, and which may sometimes be a source of difficulty from the diagnostic standpoint It is recognized that in cases of secondary metastatic deposits of carcinoma in the central nervous system the most frequent site of the primary growth is the bronchus Ferguson and Rees in 1930 reported a series of 9 cases of unsuspected primary bronchial carcinoma with secondary deposits in the brain or spinal cord In many of these there had been no obvious indication of any intrathoracic lesion, the first manifestation of illness being the nervous symptoms Many similar cases have been recorded since the publication of their paper, and in special hospitals for diseases of the nervous system X-ray examination of the chest in cases suspected of cerebral tumour has become almost a routine procedure There are numerous instances of patients brought to hospital in a state of coma, thought to be due to cerebral thrombosis or haemorrhage, or to cerebral tumour, in which subsequent post mortem

examination has shown that death was due to the deposit in the brain of metastatic tumours originating from a primary malignant growth in the bronchus which had caused no manifest respiratory disturbance during life Wyburn-Mason has recorded 3 cases of bronchial carcinoma presenting as a polyneuritis, the pulmonary symptoms being completely in abeyance, the patients having come for advice solely on account of their neuritic pains

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I am inclined to think that even the most carefully compiled tables of symptoms are apt to be a little misleading since out patients are notoriously vague in their statements and descriptions which are prone to variation on

different occasions and with different examiners My own clinical observations have led me to differ in some respects from the view of the relative diagnostic importance of symptoms that might be deduced from the more formal statistical investigations

Dyspnoea in my opinion is one of the most prominent among the earlier symptoms of bronchial carcinoma and on the whole it is one on which I have tended to place considerable reliance in the clinical examination of these patients It not infrequently appears to be incommensurate with the objective evidence of thoracic disease It should be regarded with particular suspicion, for example, in any patient of bronchitic type in whom there is no evidence of cardiac insufficiency or of marked emphysema, and where physical signs are absent or disproportionate to the severity of the symptoms The explanation of this dyspnoea has always been a matter of some difficulty Some interesting observations have been published on the subject by Rienhoff in a commentary on the results of treatment in a series of 181 consecutive cases of primary lung cancer In his analysis he mentions hyperpnoea [*sic*], which comes only fifth on the list of signs and symptoms, as occurring in 23 per cent of the patients in this series He describes it as 'a sudden desire to breathe in deeper breaths, not exactly similar to air-hunger, but approximating to this condition ' As a possible explanation he suggests that occlusion by a plug of mucus of a secondary or tertiary bronchus, already partly blocked by an intrabronchial growth, may give rise to obstructive emphysema of the corresponding pulmonary segment, with consequent reflex disturbances in the rate and amplitude of the respirations That such bronchial occlusion can be responsible for marked dyspnoea or hyperpnoea, if only temporary, is obvious from the experience of many patients who suffer from chronic bronchitis especially the plastic type, and Rienhoff's suggestion is undoubtedly supported by careful clinical observation

So much for the dyspnoea of the earlier cases In the later stages of the disease severe breathlessness is a common complaint, apart altogether from the respiratory embarrassment due to a large pleural effusion It may be paroxysmal, and is not infrequently a result, apparently, of movement or change of posture This may possibly be due to pressure on the cardiac branches of the vagus, in view of the altered mechanical conditions within the chest, on the other hand it may, as some have suggested be a reflex associated with abnormal position or movements of the mediastinum In the last stages when there is a huge mass of growth filling an entire hemithorax, dyspnoea from pressure may be very great The most distressing examples, perhaps, are seen in the condition described by Assmann as 'lymphangitis carcinomatosa', in which, though there may be no stenosis of a main bronchus, there is a cancerous invasion of the peribronchial and peri-

vascular lymphatics, which produces a certain degree of spasm and also hinders pulmonary ventilation by infiltration of a large number of alveoli He notes that primary bronchial carcinoma does not as a rule cause such an extreme degree of respiratory disturbance because the lymphangitis carcinomatosa in the neighbourhood of the primary tumour, though frequent, is generally not so extensive and spares large portions of the lung, at any rate on one side The most striking examples of dyspnoea and cyanosis, without stenosis of a large bronchus, are to be found in cases of so-called miliary carcinomatosis, which is usually secondary to carcinoma of other organs, especially the stomach (cf Fig 104, Chap XI)

Cough is extremely variable, both in its character and in its severity Practically all these patients complain of cough at some stage of their illness, but here again I am inclined to distrust the evidence of tabular statistics as a practical guide to the importance of this symptom, at any rate in early cases Most patients, whatever their malady, will confess to cough, certainly in answer to a leading question What is of greater significance is the admission that there has been some recent alteration in the character of the cough by a patient who has had chronic cough for years In late cases, of course, cough may be increasingly troublesome, either from involvement of the pleura, or possibly from pressure of the growth on the laryngeal nerves (as in aortic aneurysm) Involvement of the recurrent laryngeal nerve may also occasion some hoarseness

Pain is a variable symptom As in cancer generally, I should not describe it as a prominent feature, though in advanced cases it may be severe, and may sometimes occur in sudden paroxysmal attacks which come on at intervals for no apparent reason This not infrequently happens with surprising regularity at certain hours of the day or night In the earlier stages although pain may be experienced, it is seldom very bad except perhaps in the case of growths high up in the thoracic inlet involving the first rib with occasional infiltration of the vertebra In some cases there may be localized pain due to involvement of the pleura

Haemoptysis, though by no means a constant or even a very frequent initial symptom is one of the most important as an unequivocal indication for further and complete investigation I have constantly had occasion to issue the warning that the occurrence of a slight haemoptysis in a middle aged or elderly patient may be the first sign of a bronchial carcinoma, and moreover that this symptom may be and often is unaccompanied by any abnormal physical signs in the chest or even by any very obvious departure from the normal appearances in the radiogram I would once more reiterate that no such patient who comes for advice on account of definite blood-spitting, however slight in amount, should be given a final reassurance until complete

investigation of the cause has been carried out, and that of all the methods of investigation bronchoscopy may be, and often is, the only one which leads to the recognition of a primary bronchial carcinoma, endo-bronchial or extra-bronchial A frequent story is that of recurrent small haemorrhages, varying in amount from a slight staining of the sputum to expectoration of a few drachms of blood Profuse haemoptysis in the course of the disease is uncommon; when it does occur it is mostly as a terminal event, due to ulceration of growth into a large vessel, and followed by death within a few minutes

Sputum is usually scanty in the early stages, but may become copious later on, this is especially likely when bronchiectatic changes have developed in a portion of the bronchial tree distal to a branch which has become partially obstructed by the growth This may be followed by breaking down of the lung tissue, with secondary infection and general constitutional disturbance The occurrence of pyrexia, which characterizes a number of cases of lung cancer, is usually due to this cause, and is, generally speaking a relatively late phenomenon in the clinical course of the disease

Weakness and Loss of Weight. General weakness is a not uncommon complaint which tends to increase as the disease progresses, but loss of flesh is by no means a constant feature, in fact the good nutrition and general *bien être* of so many of these patients, even at a fairly late stage of the disease, are often surprising Occasionally one sees marked and rapid loss of weight, but this is far less frequent than might be expected, and absence of the wasting and cachexia, so characteristic of pyloric cancer and cancer in many other sites, cannot be taken as rendering a diagnosis of primary bronchial carcinoma unlikely, where other reasons for suspecting its presence already exist

Physical signs and X-ray Examination. From what has already been said about the anatomical aspects of bronchial carcinoma and the way in which these growths tend to spread it will be evident that no single picture can be drawn of the patient's physical condition, which obviously varies according to the size and position of the tumour and the particular stage of its development The clinical picture of a patient in the very advanced group to which I have already referred is one which can hardly be mistaken The extreme degree of dullness over the whole of one side of the chest which is entirely occupied by a large mass of growth, might at first be attributed to a large pleural effusion, but the position of the heart should make this distinction clear, since the displacement of the heart to the opposite side by an effusion of such extent would easily be recognizable Vocal resonance and tactile vocal fremitus are absent, as the main bronchus in these circumstances would almost inevitably be completely occluded The signs of gross venous obstruction, already mentioned, in addition to the other details of the picture, would

suffice to render the diagnosis sufficiently obvious It is not, perhaps, very often that the practitioner is called in for the first time to see a patient in this desperate condition, but it does occasionally happen, and for this reason I have felt it necessary to make some reference to it

In a large proportion of cases the doctor is first consulted at a stage of the



FIG 57 Radiogram from a case of bronchial carcinoma (upper lobe type) (From Davidson s *Practical Manual of Diseases of the Chest*)

disease which though not really early and operable, is still not very advanced, and the clinico radiological picture in such cases can be conveniently divided into three main groups (1) the upper lobe type, (2) the lower lobe type, and (3) the peripheral type *This description is based mainly on the radiological* appearances It must be understood that the latter are likely to show considerable variation not only in different cases, but also at different stages of the disease in the same patient, but for practical purposes it is possible to describe certain main features by which most of these cases are characterized

Fig 57 illustrates a very typical example of a right upper lobe collapse due to obstruction of the upper lobe bronchus by carcinoma Fig 58 shows a

similar state of affairs affecting the lower lobe The peripheral type (Fig 59) was at one time cited in support of the hypothesis that primary carcinoma might arise in the alveolar parenchyma, a view which is no longer regarded as tenable, the growth in this type of case being presumed to start in the mucosa or in the submucous tissue of one of the smaller peripheral branches of a bronchus and to spread gradually into the lung tissue



FIG 58 Radiogram from a case of bronchial carcinoma (lower lobe type) (From Davidson s *Practical Manual of Diseases of the Chest*)

The signs given by the ordinary clinical method of percussion and auscultation are greater or less according to the degree of pulmonary collapse that has resulted from the bronchial obstruction In many cases there is some impairment of resonance over the area corresponding to the collapsed lobe, with diminution in the air entry and weakness of the respiratory murmur The breath sounds may be somewhat bronchial in character, as in any condition in which there is some consolidation of the lung from whatever cause Evidence of airlessness of a portion of the lung from broncho stenosis will, however, often appear in the radiogram before it becomes obvious on physical

examination In the peripheral types of growth one is much less likely to find physical signs of any significance, and diagnosis in such cases will depend more than ever on the X-ray appearances taken together with the clinical history and corroborated by the various other methods of examination which have now become more or less a matter of routine



FIG 59 Radiogram from a case of bronchial carcinoma (peripheral type)

Clubbing of the fingers is not uncommon but is by no means invariable, as a diagnostic feature it cannot be regarded as of great significance Paralysis of one side of the diaphragm from involvement of the phrenic nerve by the tumour and slight hoarseness from involvement of the recurrent laryngeal nerve are often seen, these are late rather than early features, but they not infrequently occur in patients whose general condition is good and who have not complained of any great respiratory embarrassment Localized oedema is

usually a late sign, as is enlargement of the lymph-nodes in the supraclavicular region or in the axillae, the latter, however, has been seen in cases in which there was little clinical evidence that the disease was far advanced

The description given so far of the objective evidence of lung cancer has been based on the general symptomatology common to most cases, and the appearances seen in an ordinary tele-radiogram, classified into the three main groups above mentioned When the main primary growth is either endobronchial or in the hilar region in the neighbourhood of a bronchus, the radiological shadow is likely to be lobar or at any rate segmental, since it represents the collapsed area of lung parenchyma corresponding to the obstructed portion of the bronchial tree In the peripheral types of growth the opacity seen in the lung-field is likely to vary considerably in size, shape, and definition, according to the nature and anatomical relations of the growth itself

However strong the presumptive evidence of bronchial obstruction, this can only be demonstrated by further examination, e g by bronchography or tomography, and by bronchoscopy I have already indicated (Chap I) that bronchoscopy has tended in recent years to replace bronchography to a large extent This does not, of course, mean that the bronchogram has not still a place of some importance in the investigation of these cases, especially, as Rienhoff observes, in demonstrating the obstruction of a bronchus by a small growth which may not have shown an obvious shadow in an ordinary radiogram Some of the various radiological pictures that may be shown are seen in the following illustrations (Figs 60 to 75) The clinical history of these cases is briefly as follows

Figs 60, 61, and 62 illustrate the typical appearance of a 'blocked bronchus' in cases of advanced carcinoma These bronchograms were obtained from 3 patients in whom a large bronchus had been practically obliterated by a mass of growth, the corresponding area of lung having been rendered airless and having therefore collapsed

Fig 60 shows the so called 'rat-tailed' type of blocked bronchus (right lower lobe), Fig 62 a similar picture (right lower lobe) In Fig 61 the left main bronchus is completely obstructed

In all these patients the condition was inoperable

Figs 63 and 64, W W a man aged 56, had an attack of influenza [sic] in September 1939 He was in bed for a week with a high temperature In the course of a few weeks he lost a stone in weight and, as his cough and expectoration persisted after the febrile attack, pulmonary tuberculosis was suspected In the course of time the cough improved a little, but he complained of dyspnoea, he was therefore sent to Brompton for further investigation

On admission he was found to have dullness with absent breath sounds,



Fig 60 Bronchogram from a case of bronchial carcinoma showing blocking of right lower lobe bronchus (fat tail type)



Fig 61 Ditto showing block of left main bronchus



Fig 62 Ditto showing block of right lower lobe bronchus

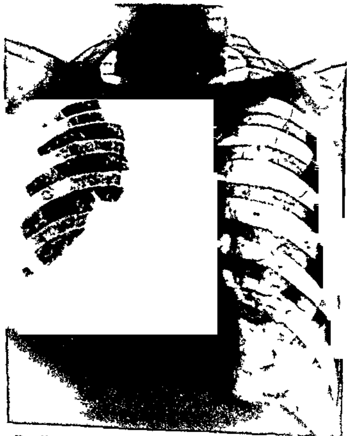


Fig 63 Right lower lobe collapse due to obstruction of bronchus by carcinoma

Fig 64 Same case as Fig 63 *Bronchogram showing blocked* bronchus

vocal resonance and vocal fremitus at the right base No enlarged lymph nodes were felt in the supraclavicular or axillary regions His vital capacity was 2 000 c c

Bronchoscopy was performed on *January 19th 1940 with the following* result Cords move equally carina normal At the level of the middle lobe

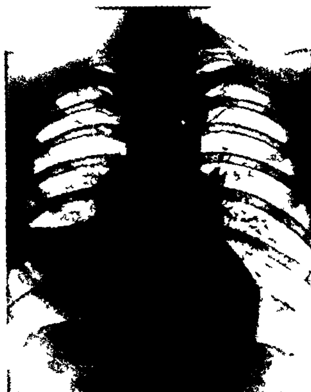


FIG 65 Radiogram from a case of bronchial carcinoma showing collapse of right middle lobe

bronchus but hiding it and the lower lobe orifice the whole lumen of the right bronchus is occupied by a soft mass which bleeds on touching Large pieces were taken for biopsy The pathological report on this specimen was as follows The microscopical appearances of these fragments of bronchial mass are those of a carcinoma of the oat cell type

On February 2nd an exploratory thoracotomy was carried out The posterior portion of the right lower lobe was occupied by a large stony hard tumour approximately 2 inches in diameter and with an irregular outline

On palpation several hard nodules were felt, extending in the pleura to the pericardium Similar nodules could be felt in the region of the inferior pulmonary veins The condition was therefore regarded as inoperable and the chest was closed

Figs 65, 66, and 67 C H , a man aged 55, was seen in the out patient department at Brompton with a history of cough and sputum persisting after a febrile attack 3 months before There had been about 10 lb loss *in weight* Examination of the chest showed dullness to percussion at the right base He was admitted shortly afterwards, and on April 19th 1940 bronchoscopy was performed with the following result 'Larynx and carina normal There was no abnormality detected in the bronchial tree the openings of all the bronchi that could be seen were normally patent there was a small amount of muco pus in the right main bronchus ' Bronchoscopy was repeated on May 5th, *the appearances being exactly the* same as at *the* previous examination

The patient was discharged home on June 2nd, but in July he began to complain of headaches which got steadily worse eventually he developed *a divergent squint and was found to have some weakness of the left internal* rectus No appreciable change was seen in the X-ray appearances in the chest Ultimately he developed a left hemiplegia and signs of pericarditis, and died *Autopsy showed a large mass of growth obstructing the right middle* and lower lobe bronchi and involving the pericardium Secondary nodules were found in the suprarenals

Figs 68 and 69 W L , a man aged 60, gave a history of an influenzal attack [*sic*] in January 1940 This was succeeded by cough with sputum and later by an attack of sharp pain in the right side The pain lasted only 3 days The cough improved When seen in Brompton in September 1940 he had lost the above symptoms, but was complaining of some lassitude and had lost a little weight On examination there were no physical signs of importance in the chest there was some clubbing of the fingers

Bronchoscopy was performed the appearances being as follows 'Larynx and carina normal main bronchus normal There is a mass of growth projecting from the right middle lobe bronchus a portion of which was removed for biopsy (see Fig 70) Ten 2 0 m c radon *seeds were inserted into* and around the remains of the tumour The pathological report on the biopsy material indicated that the growth showed appearances characteristic of a squamous celled carcinoma

Bronchoscopy was repeated on November 26th *and showed only a* rough area visible in the middle lobe bronchus Radon seeds were again introduced

Two examples may be *quoted of cases in which the* preliminary investiga tions led to exploratory thoracotomy, and to attempts to remove the growth, in both instances disappointing as regards ultimate results



Fig 66 Same case as Fig 65 right lateral view



Fig 67 Bronchogram same case as Fig 65 The opaque oil has not entered the middle lobe bronchus which is obstructed by growth

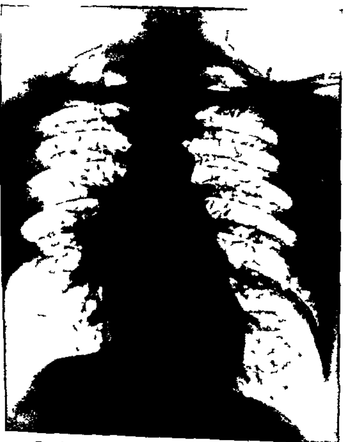


FIG 68 Radiogram from a case of bronchial carcinoma



FIG 69 Bronchogram same case as Fig 68 The opaque oil has not entered the dorsal lobe bronchus which is obstructed by growth

Figs 71 to 73 J C W, a man of 57, had been in fairly good health until the winter of 1944–5 when he began to complain of cough and expectoration

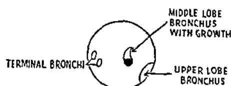


Fig 70 Diagram showing the bronchoscopic appearances in the case illustrated by Figs 68 and 69



Fig 71 Radiogram from a case of bronchial carcinoma

with occasional staining of the sputum Previous to this he had had a more or less chronic cough of which he had taken little or no notice, though he had had a slight haemoptysis in 1940 The rounded opacity in the left lower zone seen in the lateral view to be situated anteriorly was thought to indicate a



FIG 72 Same case as Fig 71 left lateral view



FIG 73 Tomogram same case as Fig 71 Showing breaking down and excavation in the centre of the growth

breaking-down peripheral growth, this was further substantiated by the tomogram

Bronchoscopy on July 31st, 1945 gave a good view of the whole of the bronchial tree and no abnormality was observed The patient was operated upon on August 28th when the lung was found adherent to the pericardium which had been invaded by growth There were enlarged hilar lymph nodes A dissection pneumonectomy was carried out and the area of infiltrated pericardium was excised The patient was discharged home on October 24th, but died at home about 3 months later

Pathological examination of the pneumonectomy specimen showed a large tumour occupying the lingula and spreading directly into the upper lobe The middle lobe bronchus was obliterated and there were nodules of growth spreading upwards into the main bronchus The lower lobe showed emphysematous change but no growth The parabronchial, hilar, and paratracheal glands were all enlarged and infiltrated by growth

Sections of the peripheral part of the tumour showed an anaplastic undifferentiated carcinoma growing freely in the bronchi and alveoli Mitotic figures and atypical mitoses were very frequent The pericardium was infiltrated by growth

Figs 74 and 75 E R S, a man aged 47, was referred to Brompton on December 12th, 1939 with a history of having begun to cough up blood at the beginning of October For the previous 2 weeks he had had some fever and had complained of pain in the left side The ordinary X-ray film showed a rounded opacity in the left middle zone, which was seen in the lateral view to be lying posteriorly, a small pleural effusion being visible at the base A barium swallow revealed no actual obstruction of the oesophagus but some spasm at the lower end was apparent In the bronchogram it was seen that the neo hydriol had not entered the opaque area and it was thought that there was some obstruction of the dorsal lobe bronchus

Bronchoscopy was performed on November 1st the report being as follows 'Larynx and carina normal There was a rounded smooth projection into the lumen of the left descending bronchus, situated on the medial wall, about 2 inches below the carina and about ¾ inch below the opening of the left upper lobe bronchus '

A biopsy specimen was obtained which on microscopic section showed appearances characteristic of a bronchial carcinoma The masses of cells varied greatly in size and shape The cells were cylindrical rather than squamous mitoses were numerous and many areas of necrosis were present

On November 10th the patient was operated on and a left pneumonectomy was carried out There was a firm hard mass, about 3 inches in diameter, in the dorsal lobe, and a larger mass occupied the hilum and tissues beneath



FIG 74 Radiogram from a case of bronchial carcinoma simulating the appearances of a circumscribed benign tumour



FIG 75 Same case as Fig 74 left lateral view

the arch of the aorta The regional lymph-nodes removed at operation showed no evidence of malignancy

This patient died on November 21st, 11 days after the operation

I have so far dealt with cases in which the disease, though not necessarily affording evidence of gross structural damage of the thoracic viscera, was yet so far advanced as to render any major operative treatment impracticable or ineffective It remains to say something of the really early case and to discuss the criteria by which it may be possible to recognize it It must at the outset be frankly admitted that in the present state of our knowledge we have no data sufficient to furnish us with any categorical rules of procedure comparable to those which can be urged for the early diagnosis of, say, pulmonary tuberculosis, in which such striking and unmistakable advance has been made in the last few years I can only remind my readers that, as Rienhoff has aptly expressed it '*there are no characteristic signs and symptoms of primary carcinoma of the lung this lesion masquerades as many of the commoner disorders of the lung*' and that, in the words of Brock '*if we are to diagnose this grave and fatal condition in a reasonably curable phase, it must be remembered that the slightest departure from normality in the lungs and bronchi is suspicious and needs pursuing*' These statements are beyond dispute Of the early diagnosis and successful treatment of primary lung cancer we can as yet cite but a few examples among the many thousands of cases of this disease with which we are now called upon to deal If the hope of substantial improvement of the present position is to be realized, we must at all costs impress upon the medical profession and the public alike the need for a much more frequent and complete investigation of the suspicious case by all available modern methods What then are we to regard as a suspicious case? It need hardly be said that a certain sanity of outlook must be preserved in this respect We cannot submit every patient to bronchography and/or bronchoscopy after the first interview, but the value and importance of these are still not recognized as fully as they should be, especially in the case of those patients with an insidious history who have not yet been driven in panic to their medical adviser by the dramatic onset of haemorrhage Even then they are too often dismissed with an unjustified reassurance because of the absence of abnormal physical signs in the chest or of gross distortion of the normal radiological picture In these same cases the previous history, when ascertained by a careful examiner, is often illuminating —to quote Brock once again 'When an alarming symptom such as haemoptysis compels attention, the story may be obtained of a premonitory cough, extending back over many months, but treated symptomatically or not at all '—All authors of experience have emphasized the importance of the nature of the cough in bronchial carcinoma and especially of any comparatively sudden change

noticed in the character of a cough that has been present for a considerable time Churchill in an analysis of symptoms notes in 10 to 15 per cent of cases the occurrence in the early stages of a wheeze [sic] which may be transient, and which differs from the wheezing of asthma or of simple chronic bronchitis in that it may be localized and unilateral, a feature that may be recognized both by the patient and by the medical man We have already referred to dyspnoea as of special significance if it is incommensurate with the objective evidence of disease on ordinary clinical examination

The abuse of the expression 'unresolved pneumonia' is one of the dangers to which at this point we may with advantage again direct attention More than 10 years ago this was emphasized by McGibbon, Baker-Bates, and Mather, who recorded an interesting series of cases in which a diagnosis of unresolved pneumonia had been made and which were subsequently examined by them with the bronchoscope Of all these patients 8 were found to be suffering from bronchial carcinoma 1 from an extra bronchial tumour of unknown pathology, 2 from an impacted non radio opaque foreign body, 5 from bronchiectasis, one from an inflammatory bronchial stenosis 2 from lung abscess, and 18 (children) from varying degrees of incomplete bronchial obstruction apparently caused by secretions In the case histories of patients who are ultimately found to have a bronchial carcinoma one of the commonest records is a previous history of an attack of so called pneumonia or in fluenza In the great majority of instances this has been in reality a transient pneumonitis, lobar or segmental in distribution, and associated with a partial block of some portion of the bronchial tree The infection of the affected lobe or broncho pulmonary segment may be manifested by fever, the general clinical syndrome which follows resembling that of a pneumonia or one of the localized pulmonary inflammations commonly seen during a prevalent epidemic of influenzal type Even cases of empyema, following a supposed pneumonic attack of this kind, may be found ultimately to be associated with malignant new growth, infection occurs in the portion of the bronchial tree distal to the point of obstruction by the growth, and a chronic empyema may result, the fundamental cause of which may sometimes not be recognized until the autopsy, possibly after a protracted period of illness

I lay stress upon this feature of lung cancer, viz the occurrence of localized areas of collapse in the lung not because in these circumstances it is possible to predict with certainty an operable condition—this can only be settled by further investigation—but because in so many instances the occurrence of collapse is the first manifestation to the patient and the practitioner of anything seriously wrong It is true that the clinical and radiological evidence of such collapse may be the outcome of an inflammatory condition that will ultimately clear up with the lapse of time, but the possibility of a neoplastic

origin of this phenomenon *especially in patients from 45 to 65* must be entertained I regard any failure to envisage this possibility as inexcusable on the part of a physician with any pretence to knowledge of modern teaching and to experience in diseases of the chest Nothing can be more pernicious than the habit still unfortunately prevalent of watching a patient in whom



FIG 76 Radiogram from an early case of bronchial carcinoma showing segmental collapse (From Davidson's *Practical Manual of Diseases of the Chest*)

radiological examination has disclosed an opacity in the lung field of uncertain type for a protracted period with a pious resolution to repeat the X ray examination in say a month or two to see if any change has occurred

Of all the present ancillary means of investigation bronchoscopy is probably the most valuable and no patient in whom there is the slightest possibility of a growth in the respiratory tract should be denied the opportunity of benefit from its use Aspiration biopsy has been strongly recommended by some authorities and as strongly condemned as a dangerous procedure by others Microscopic examination of tissue from the lesion is of course the only

infallible method of accurate pre-operative diagnosis, but the danger of dissemination of cancer cells by implantation along the needle-track is a very real one, and in the judgement of most experienced thoracic surgeons appears generally unjustifiable

The foregoing observations will, it is hoped, give the reader some practical idea of what constitutes an early stage of primary bronchial carcinoma, and of the general mode of approach by which it may be possible to recognize it before metastatic spread of the disease renders the surgeon's efforts fruitless These points can, perhaps, be best illustrated by reference to the two following cases which form an appropriate conclusion to this chapter

Fig 76 illustrates a case, already recorded (loc cit) of a man aged 41, who, with no previous history of any appreciable disability had a slight haemoptysis Nothing abnormal was detected on physical examination but X ray examination revealed segmental collapse in the right upper zone, and the medical attendant, suspecting at once the possiblity of a new growth, made urgent arrangements for the patient's transport from the Far East to London for investigation He was admitted to Brompton, where bronchoscopic examination showed no abnormality in any part of the bronchial tree that was visible Exploratory thoracotomy was carried out on November 2nd, 1944 and the whole of the right lung was removed by dissection pneumonectomy The upper lobe of the lung appeared solid but no obvious mass could be felt within it On section of the organ a small growth was seen in connexion with the wall of the apical branch of the upper lobe bronchus Histological examination showed the bronchial mucosa to be thickened by well differentiated squamous-cell carcinoma The growth was invading most of the peri-bronchial lymphatics There was no gross enlargement of the hilar lymph nodes One of these was examined histologically and showed evidence of inflammatory reaction but no growth

This patient made an uneventful recovery and was discharged from hospital on December 23rd In view of the strictly limited location of the primary growth, the absence of any evidence of metastasis, and the histological character of the growth itself, the prognosis in this case appeared to be extremely favourable, and I felt genuinely hopeful that a cure had been achieved This man did in fact remain in good health and working up to the spring of 1947 (about 2½ years from the time of the operation) He then began to develop symptoms of dysphagia, with occasional attacks of cough and choking Bronchoscopy on July 22nd, 1947 showed that the remaining (left main) bronchus was obstructed He died a few hours after the bronchoscopy, and post mortem examination revealed a large mass of growth situated in the mediastinum between the oesophagus and the trachea about the level of the bifurcation This was evidently one of the posterior mediastinal glands



Fig 77 Rad ogram from an early case of bronch al carc noma per pheral type (From Dav dson s *Practical Manual of D seases of tl e Chest*)



Fig 78 Same case as F g 77 left lateral v ew

which must have been already the seat of a secondary deposit of carcinoma when the pneumonectomy was performed No other metastatic deposits were discovered

Figs 77 and 78 This patient, a man aged 40, had a long-standing history of bronchial asthma, from which he had suffered since childhood When first seen in consultation (September 1942) his general condition was, in striking contrast to the previous case, very poor He was dyspnoeic, complained of a loose cough and night-sweats, and had lost over a stone in weight in the past few months Shortly before the consultation he had coughed up about 8 ounces of blood

Bronchoscopy was performed and, as was anticipated in view of the peripheral situation of the opacity, revealed no abnormality in any part of the bronchial tree On September 22nd a total pneumonectomy was carried out, recovery was uneventful, and the patient was discharged home on December 14th, 1942

Pathological examination of the left lung showed a mass of growth which had already begun to break down Histological examination showed a very necrotic carcinoma In a few areas in which there was no necrosis the cells appeared to be mainly spheroidal A few squamous cells, however, were present and the necrotic areas appeared to be of this type A large hilar lymph-node was examined and showed marked inflammatory reaction and reticulosis, but no malignant deposits

The after-history of this case has been very satisfactory The man returned to his work and has led a fairly active life, though still occasionally troubled by his asthma The latest report up to the time of writing, is October 21st, 1949 when I saw him He appeared in excellent health, had recovered his normal weight and apart from occasional trouble from his asthmatic tendency had no untoward symptoms

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APPENDIX TO CHAPTER VIII

PULMONARY ADENOMATOSIS

THE disease known as pulmonary adenomatosis may be briefly considered here as a neo plastic condition though it must be clearly understood that it is quite distinct from adenoma of the bronchus to which it bears no clinical relation It is a rare disease of the lungs and



FIG 79 Radiogram from a case of malignant adenomatosis (alveolar-cell tumour) of the lung (By courtesy of Dr J Clifford Hoyle *British Journal of Tuberculosis* 1942 36 158)

has been described in a comparatively recent account by Paul and Ritchie as characterized by the development of multiple adenomatous tumours or by a diffuse hyperplasia of the pulmonary alveolar lining cells One of the features of this condition which has given rise to considerable interest and to no little discussion is its histological similarity to an infectious adenomatosis known to occur in sheep (the Jaagsieckte described by Mitchell in 1915) A not inconsiderable literature has accumulated on the subject a summary of the records of 24 cases of alveolar-cell tumour having been published by Neubuerger and Geever (loc cit) who regarded the disease though admittedly rare as perhaps somewhat commoner than has been generally supposed



FIG 80 Microphotograph same case as *Fig* 79 Showing appearances in pulmonary adenomatosis (By courtesy of Dr J Clifford Hoyle, *British Journal of Tuberculosis*, 1942 36, 158)



FIG 81 Microphotograph same case as Fig 79 Showing area of carcinomatous degeneration (By courtesy of Dr J Clifford Hoyle, *British Journal of Tuberculosis*, 1942, 36, 158)

The essence of the pathological change in the lungs is an epithelial proliferation of the cells lining the alveoli with the formation of numerous intra alveolar papillae Two forms have been described by various writers one a multiple nodular type in which scattered nodules of consolidation are seen on the surface of the lungs on section the other a diffuse type which may be lobar in distribution or may involve the whole lung on one or both sides A very complete and illuminating report of a case with a detailed discussion of the histology is furnished by Dacie and Hoyle to whom I am especially indebted for the loan of the accompanying radiogram &c and for valuable criticism and advice One of the most interesting and important of the results of their study of a large number of microscopic sections was the discovery in some of areas showing a change from the condition of papillary adenomatosis to definite carcinoma in others moreover they noted a carcinomatous invasion of the pleura the cells being similar in type to those in the carcinomatous mass seen in the lung sections A similar transition from adenomatosis to carcinoma is noted by Paul and Ritchie who to a review of the literature have added 4 cases of their own

Clinical and Radiological Features So far as can be judged from the comparatively small numbers of cases on record the disease appears to occur mostly in middle aged or elderly persons the onset being usually insidious though in some instances there have been acute respiratory symptoms The two outstanding symptoms are cough and dyspnoea the latter becoming more distressing as the condition progresses and sooner or later being accompanied by cyanosis The cough is practically always attended by expectoration of fairly large amounts of frothy mucous sputum The duration of the disease is usually lengthy occasionally it may be a matter of months more often it is several years from the first onset of symptoms until death. Treatment except for palliative measures appears to be unavailing

Radiograms of the chest show widespread patchy nodular infiltration scattered through out one or both lung fields there may also be larger densely opaque areas suggestive of more massive pneumonic consol dation The X ray appearances cannot be said to be in any way diagnostic From the rad ologist s standpoint alone they might well be confused with chronic diffuse pneumonias secondary carcinomatosis sarcoidosis or even with the widespread pulmonary infiltration seen in the less typical forms of Hodgkin s disease or other forms of reticulosis

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IX

CARCINOMA OF THE BRONCHUS

THE TREATMENT PROBLEM

IN considering the treatment of lung cancer from the practitioner's standpoint I propose to take four main aspects, (1) operative treatment, (2) radiotherapy, (3) chemotherapy, and (4) symptomatic treatment, and to discuss them briefly on broad general lines, and to some extent in relation to each other

Operative Treatment. In the present state of our knowledge it must be admitted that the only procedure which we can justifiably claim and urge upon our patients as radical is an attempt to achieve by surgical operation the complete extirpation of all malignant tissue at the earliest possible opportunity To say this is but to repeat a platitude it seems equally obvious that the thoracic surgeon must depend to a very large extent upon his medical colleagues for diagnosis of the condition at a stage in which the lesion is still localized and before metastatic spread has begun The technical details of his work have been dealt with fully in a later chapter, but I am constrained at this point to say something about the surgery of the chest from the physician s standpoint, since this monograph has been written for all who are in any way concerned with the subject of thoracic new growths, and not least for the chest physician and the general practitioner, upon whose shoulders will lie, as often as not, the primary responsibility of bringing the case to the notice of their surgical colleagues

I have referred in my introductory remarks to the duty which devolves upon the experts in chest disease of explaining to the patient or to his relatives the significance of lung cancer in terms such as will enable them to realize the true position and to form a just and objective estimate of the outlook in any case in which an exploratory thoracotomy is recommended The onus of such explanation lies, more often than not, upon the physician, and it is important that he should not rest content with a general and perhaps vague acquiescence in the possibilities of surgery in these cases, but should have a clear working knowledge of the scope and limitations of operative procedure and of some of the problems and difficulties which may confront the surgical colleague into whose hands he proposes to commit his patient I do not of course, suggest that it is necessary or even desirable to discuss in detail the statistical aspects of pneumonectomy with the lay public, who in most cases are hardly in a frame of mind to assess these at their proper value Some attempt, however, should be made to enlighten them as to the possible chances of success, so far as we can judge of these in the light of recent

figures, and as to the possible disappointments which they may have to face, even in those cases which prima facie appear to offer the most hopeful prospects We know that of all the cases of bronchial carcinoma which present themselves for investigation only a small proportion are ultimately regarded as operable, and that of those which are so regarded, again only a small proportion prove actually to be operable when submitted to the final test of exploratory thoracotomy To put clearly before the persons concerned this *vital truth, which they have every right to know before their consent to* operation is obtained, demands no little experience in the general handling of medical problems and a much greater expenditure of time and patience than is usually, in my experience, devoted to this aspect of medical practice

In the attempt to give a fair and truthful account of what the patient may expect at the hands of the thoracic surgeon one can only point out that the number of successful pneumonectomies for bronchial carcinoma has increased appreciably in the last 10 or 15 years, and that of all the patients found to be suffering from this disease a few at least can now be really cured by surgical operation Of the many statistical returns available the following brief extracts may be quoted here

Rienhoff records a series of 327 patients referred for surgical treatment at the Johns Hopkins Hospital All these were explored, and in 215 (i e in 65 75 per cent of the whole) the condition was found to be inoperable, the average duration of life of these patients after discharge from hospital being 5 months In the 112 cases (34 25 per cent of the whole) found operable the growth was removed, and of these patients 39 per cent had survived (up to the date of publication of his paper) for periods varying from one month to thirteen years

Oschner and DeBakey quote 412 cases of bronchogenic carcinoma observed over a period of twelve years Of 246 patients who were explored, 147 (i e 59 8 per cent) had a primary lung resection, that is to say 35 7 per cent of the total 412 In other words, as these authors observe, of every 3 cases of clinical lung cancer 2 will appear operable, and only 1 will actually prove to be suitable for lung resection Of their patients for whom resection was possible and on whom this operation had been carried out five or more years previously 23 3 per cent were still alive—the authors calculated an 8 per cent survival rate for all cases of lung cancer

Bjork has compiled a valuable analysis of 345 cases diagnosed and treated at the Brompton Hospital and the Royal Cancer Hospital Of 79 patients operated on and followed up, 5 per cent had survived for more than 5 years, 16 per cent for more than three years, 23 per cent for more than 2 years, and 39 per cent for more than 1 year For a full understanding of the position it is, of course, essential to peruse the original reports, but the above

quotations will suffice to give the reader some idea of the main facts in regard to the achievements of the last decade and some guide as to what can be offered to the patient in whom a diagnosis of primary bronchial carcinoma has been established

While the possibilities of operative cure of bronchial carcinoma have undoubtedly increased, so that the position today is infinitely less gloomy than it was a quarter of a century ago, it is still necessary in many cases to point out to relatives the very definite limitations within which the thoracic surgeon has to work Apart from certain phenomena which are ordinarily taken as obvious contra-indications to exploration (e g blood stained pleural effusion, diaphragmatic hemi-paralysis from direct involvement of the phrenic nerve by growth, recurrent laryngeal nerve paralysis, evidence of widespread metastasis) there are not a few cases in which, though they have shown no gross distortion of any part of the bronchial tree on bronchoscopic examination, and in which the growth was thought to be localized, exploratory thoracotomy has revealed a condition hopeless in view of the presence of numerous secondary deposits, and the chest has had to be closed forthwith For this reason it is only just that when an exploratory operation is advised, even in what appear to be the most hopeful circumstances, some warning should be given beforehand of the possibility of disappointment

It has been my experience that direct and awkward questioning on the part of the patient himself is the exception rather than the rule, and that when told that the preliminary investigations are designed to enable a decision as to the form of treatment, operative or non-operative, that should be advocated, he usually acquiesces without demur Occasionally, however, one is faced with a blunt request for the truth, the whole truth, and nothing but the truth, in such circumstances I have seldom, if ever, refused to supply the demand for details, however unpalatable

Radiotherapy. What I have already said in regard to the achievements of thoracic surgery in improving the prospects of the patient with bronchial carcinoma must be taken also to refer to radiotherapy, of which it may be said without doubt that it is now possible to apply it to these lesions with much greater effectiveness than was the case some years ago In the earlier days of deep X-ray treatment the general effects of the radiation, apart from the local action upon the tumour itself, were often very distressing Patients complained of a feeling of considerable exhaustion, and in some instances vomiting occurred Although inoperable cases continued to be referred to the radiotherapist for treatment, this was often more in the nature of a gesture than an expression of any real faith in the value, actual or potential, of the work of the X-ray departments It is only fair to recall the disappointing experiences of those surgeons who first urged, on principle, more frequent

exploration of the chest in cases which were then rightly regarded as hopeless Research into the best methods of applying deep X-rays had been proceeding *pari passu* with the work of the thoracic surgeon, though possibly with a somewhat slower rate of progress The somewhat drastic effects of X-ray treatment to which I have just referred were, perhaps, inevitable at a time when experimental radiotherapy was still, so to speak, in the stage of adolescence, a stage through which thoracic surgery also had to pass Nevertheless, the pioneers of X-ray treatment in diseases of the chest whose vision of possible developments in their own speciality was at least equal to that of their colleagues in the surgical field, maintained their ground undeterred by such difficulties Two things have emerged as a result of the immense amount of physical and clinical research that has been carried out in the best radiotherapy departments The first of these is the achievement of a technique that enables the most effective dose of radiation to be given to the actual tumour area with the minimum disturbance of the surrounding tissues. Seldom, if ever, does one now see the gross reactions and depression of the patient's general resistance and well-being which frequently characterized earlier efforts in the radiotherapy of malignant disease The second, and perhaps the more important, is a realization of the possibilities in regard to the use of radiation in combination with surgery, especially as a pre operative measure, in cases which might at first be regarded by the surgeon as inoperable for one reason or another Of this it is, perhaps, premature to speak except in very general terms but there does seem to be good reason to hope that with further research, on lines with which radiotherapists are now familiar, and with increased co-operation and team work between the surgical and radiotherapy departments, the result of such combined treatment in bronchial carcinoma may ultimately show an appreciable reduction in the mortality from this disease

The statistical aspects of radiotherapy, with critical analysis of the figures for various groups of cases have been set forth in detail by Professor Smithers in the chapter which follows this It is of some importance that the practitioner should be in a position to see the results of X-ray treatment, no less than those of radical thoracic surgery, in their true perspective, and in the interests of his patient to realize with some measure of accuracy the scope and limitations of both these methods of approach In frankly inoperable cases radiotherapy has a very real value as a palliative, at the same time it must be remembered that it is by no means always applicable As in other forms of treatment, there are circumstances which if they do not contra-indicate its use entirely, may materially affect the dosage and the duration of the course of treatment in different cases Such considerations are fully discussed and explained in Chapter XIII

Chemotherapy. The use of various chemical preparations in the treatment of cancer has been a subject of experiment for many years The results in bronchial carcinoma can only be described as disappointing but some reference must be made to the subject here, if only to give an indication of the lines on which chemotherapy has been attempted

In the earlier days of the treatment of intrathoracic malignant disease various salts of the heavy metals were used in inoperable cases In the Brompton series (1930) of 107 cases there are records of the employment of such remedies in 4 cases In 2 cases uranium was used the first patient received in the course of a fortnight 3 intravenous injections of collosol uranium, the second had 11 injections consisting of 5 c c of a radio-active solution of uranium with 5 c c of a 5 per cent solution of sodium citrate In the other 2 cases 2 c c and 5 c c respectively of a solution of lead selenide were administered intra venously In none of these 4 cases was any benefit observed, nor were there any untoward effects

Since that time a great deal of work has been and is still being carried out on the chemotherapy of malignant disease, but so far in cases of lung cancer no really effective results have appeared comparable to those seen in malignant disease of the breast or prostate after administration of hormones The remedies chiefly employed in thoracic cases have been the chloro ethylamines and urethane The most hopeful results from these have been seen in Hodgkin's disease, and also in leukaemia Temporary improvement has been observed in a few cases of lung cancer after administration of nitrogen mustard (methyl-bis [B chloro ethyl] amine hydrochloride), but in no case has this been certainly due to any direct effect of the drug on the tumour

Some reference must be made to the observations of Gaensler and others on the cytological changes in bronchogenic carcinoma following treatment with nitrogen mustard In 8 of their cases the microscopic changes after treatment were mainly giant cell formation, nuclear fragmentation, increase in mitosis and production of atypical mitosis These are the details noted in cases of well differentiated tumours in the undifferentiated growths a decrease in the numbers of mitoses was observed as well as the appearance of large areas of necrosis In 4 additional cases these authors found a disappearance of the growth from affected lymph nodes and from the bronchial tree, and an absence of any evidence of remaining growth, fibrosis, or necrosis on section of areas involved before treatment In their record of clinical results they note objective evidence of improvement in 54 per cent of 60 cases of bronchogenic carcinoma treated with nitrogen mustard In the cases so treated such improvement was noted in 83 per cent of undifferentiated tumours, in 50 per cent of squamous cell tumours in 33 per cent of adeno carcinomata, and in 11 per cent of epidermoid [sic] tumours It is difficult to assess the practical

value of this work It would appear from the observations of other research workers that the variation from part to part in untreated tumours is at least as great as that observed in treated tumours and attributed to the effects of the drug

In 1944 a joint clinic of the Brompton Hospital and the Royal Cancer Hospital was established for the investigation of the treatment of inoperable bronchogenic carcinoma by radiotherapy and also by chemotherapy The total number of patients treated by chemotherapy up to date is 75 Of these advanced cases 54 have been treated by chemotherapy alone (7 with urethane, 4 with dinoestrol, and 43 with chloro-ethylamine) One patient was treated post-operatively with chloro-ethylamine and lived for 9 months Twenty patients were treated by chemotherapy and radiotherapy combined (1 of these subsequently had a pneumonectomy and was alive 7 months later, 2 others were still alive at the last follow-up 30 months and 27 months respectively after treatment)

Of these 54 patients treated by chemotherapy alone 1 was still alive at the last follow-up, 21 months from treatment, another was alive 14 months from treatment Of the remaining 52, 49 were known to be dead, and 3 had been lost sight of The 49 known to be dead lived an average of 5 4 months after starting treatment Approximately half the treated persons gained some symptomatic relief but in many this lasted less than 1 month The majority vomited after treatment, one patient vomiting repeatedly for 11 days after a single injection of nitrogen mustard this patient, as the result of aspiration of vomited material, developed collapse of the whole of the right lung he remained alive, however, for 14 months Two others refused to continue with this treatment, but two of the three were having radiotherapy in addition In a few cases symptomatic improvement was striking One patient with an oat-cell carcinoma, who had severe obstruction of the superior vena cava, was very seriously ill, but obtained rapid relief from the venous obstruction after one injection He then relapsed and was given a second injection, from which, however, he derived less benefit At this stage he was well enough to be given X-ray therapy and he lived for 9 months A pleural effusion (? following exploratory thoracotomy) was absorbed in one patient with a squamous-cell carcinoma, this was, unfortunately, one of the three already mentioned who could not be traced after the completion of the treatment One man with gross hypertrophic pulmonary osteo-arthropathy had been attending a rheumatic clinic and was complaining of joint pains cough and haemoptysis after the first two of four injections of nitrogen mustard his pains were relieved completely, his haemoptysis ceased, and he gained 12 pounds in weight This man remained fairly well for 6 months, his symptoms then returned, and he died 3 months later

From observations up to date of the effects of these chemical agents on bronchial carcinoma it would hardly appear that their use has been vindicated In conclusion, a brief reference may be made to the sulphonamides, which have some place in the treatment of cases of lung cancer in which toxaemia due to breaking down of the growth with superadded infection has contra-indicated, for the time being at least, the employment of deep X-ray therapy In some instances a preliminary treatment with sulphonamide drugs has enabled the radiotherapist to give a course of radiation at a later date, when the toxaemia has been successfully combated and the patient's general condition has to some extent improved

Symptomatic Treatment. From what has already been said it will be clear beyond doubt that the treatment of choice in lung cancer, where possible, is surgical The value of X-ray therapy in the relief of certain symptoms and in its capacity, up to a point, to postpone the inevitable end and to prolong to a varying extent the span of tolerable life is indubitable While up to the present we have no justification for regarding it as anything but a palliative, the latest work has suggested that, in combination with surgery, it may in the future play a more important part in treatment There remain for consideration the large numbers of patients who, having reached the stage at which no surgical treatment is possible and for whom radiotherapy is no longer advisable, are beginning to suffer the constant discomfort and misery which attend the last phases of this disease and for whom something must be done by way of relief Symptomatic treatment is a subject neglected in most text books, but it still remains an essential duty of the medical profession, and the regular medical attendant in an advanced case of bronchial carcinoma has the right to look to the specialist for advice and effective help in such circumstances, no less than for technical knowledge and skill in operable cases

The two chief symptoms with which the doctor is most frequently called upon to deal in the late stages of lung cancer are pain, and the respiratory distress associated with gradually increasing asphyxia I have already said that pain is, as a general rule, less prominent in these patients than in those dying of cancer in some situations other than the lungs In fact it is usually only in the last phases of all that it appears Severe pain may, however, then occur, sometimes from pleural involvement, sometimes from extension of the disease to bone and periosteum, for example in case of metastatic deposits of growth in the ribs, &c , and especially in case of direct extension to ribs and vertebrae, as in growths high up in the thoracic inlet (the so-called Pancoast superior sulcus tumour)

The prescription of anodynes calls for no little skill and judgement In the earlier stages much comfort can be got from Veganin and other similar preparations of codein in combination with antipyretics Pethidine is a

popular remedy, which is generally found to be efficacious Sooner or later morphine or its derivatives may become necessary and should not then be withheld The disadvantages of repeated hypodermic or intramuscular injections in private practice are sufficiently obvious both from the busy practitioner's point of view and from that of the relatives A tablet of morphine, gr $\frac{1}{4}$ or gr $\frac{1}{2}$, dissolved under the tongue, is often rapid and effective in its action A combination of morphine and cocaine is, in my experience, valuable not only in the control of pain and general discomfort but also in the production of a state of euphoria which is a blessing alike to the patient himself and to his relatives The following prescription has for a long time been in use in the Brompton Hospital

Morphine	gr $\frac{1}{4}$
Cocaine Hydrochlor	gr $\frac{1}{4}$
Spts Vini Rect	ʒj
Syr Aurantii	ʒss
Aq Dest	ad ℥ss

As soon as it is evident that drugs of a milder type are insufficient to afford the necessary relief, the above should be prescribed In most cases it is enough to order it twice daily Later on it may be increased in amount and or in frequency, as experience may dictate

In cases in which pain occurs from pleural involvement the introduction of air into the pleural cavity has occasionally proved an effective remedy It is not very often that resort is had to this, but I have seen it used on occasions, and regard it as a therapeutic measure which may sometimes be of practical value and which is therefore worthy of mention In some instances of referred pain, relief may be afforded by injection of alcohol around the intercostal nerves near their origin, in extreme cases the operation of chordotomy with destruction of the spino thalamic tract has been effective It is seldom that such drastic measures as the latter are called for

The gradually increasing asphyxia, with cyanosis and grave respiratory embarrassment, is one of the commonest and most distressing features of this condition Oxygen administration, either by means of the B L B mask, or through nasal catheters on a Tudor Edwards carrier, may be urgently called for Some of the worst examples of respiratory distress are seen in the lymphangitis carcinomatosa due to miliary deposits of secondary growth throughout the lung fields Although oxygen may give some relief the use of morphine, with or without cocaine is usually necessary in addition

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X

NON-EPITHELIAL MESOBLASTIC GROWTHS

SARCOMA AND ENDOTHELIOMA

IN an earlier part of this volume (Chap VII) I drew attention to the difficulty surrounding the problem of the accurate histological classification of primary malignant growths of the lung and bronchus and referred by way of example to the ultimate recognition of the so-called lympho-sarcomata of the mediastinum as anaplastic carcinomata (Barnard's oat-celled tumours) This difficulty appears to me to have been greater with the non epithelial growths than with the obvious carcinomata, and the considerable variation in opinion evident among recognized authorities in microscopic anatomy has given rise to much uncertainty in the minds of clinicians and at times to a state of confusion which has seemed almost chaotic

Much of our former ignorance of the true nature of disease must be ascribed to the apotheosis of classification as an end in itself, and to this the clinicians of former generations were especially prone As this habit of thought was gradually replaced by a tendency to think of disease in terms of general pathology rather than as a series of more or less isolated pictures, separated from each other by a sterile if convenient nomenclature, our understanding of the essentials of many clinical problems became clarified and our knowledge not only of pathogenesis but also of treatment was correspondingly simplified This is undoubtedly true of the clinical side of medicine, and in recent years there seems to have been a similar tendency in the domain of histology

In a work of this kind, which attempts primarily to deal with the diagnostic and therapeutic aspects of thoracic tumours, I make no pretence of any but the most elementary knowledge of the histological problems relevant to the subject, nor any assumption of authority in matters which necessarily lie outside my proper province Some reference, however, must be made to histological classification, about which, as I have just observed, there has been so much dissension, which can hardly have failed to retard the satisfactory fulfilment of our common task of accurate diagnosis and treatment. It is with this in mind that I welcome any account of these growths which tends towards simplification of the over-elaborate descriptions encountered in many works on morbid anatomy and histology The essence of the matter is, I feel, rendered much more intelligible by Willis's definition of a sarcoma as '*a malignant tumour arising from any non-epithelial mesodermal tissue, fibrous, mucoid, fatty, osseous, cartilaginous, synovial, lymphoid, haemo-poietic,*

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The pure sarcomata (round-celled, spindle celled, &c), which are vascular and highly malignant mesodermal growths, occurring more often in young than in old subjects, are found in the lungs mainly as secondary deposits disseminated via the blood stream from a primary sarcoma elsewhere in the body (e g bones, &c) True primary sarcomata of the lung have been recorded, but there is no doubt that they are extremely rare, the incidence ascribed to them in some of the older literature must be attributed, as we have already indicated, to histological misconceptions which have since been corrected Two cases have been quoted which presented as empyemata One of these, reported by Baumann and Bainbridge, was a child of 4 who had been admitted to the Hospital for Sick Children the empyema having been confirmed by exploratory puncture After death the upper lobe of the left lung was found to be replaced by a soft growth, which on microscopic examination was pronounced to be a sarcoma the bronchial and mesenteric glands were apparently healthy, nor were any other tissues or organs in the body involved The other case occurred in a man of 47, recorded by Jessop This patient was admitted to hospital with a left-sided empyema, which was treated in the usual way by rib resection and drainage Seven weeks after the operation the patient's condition became worse and enlargement of the liver was noted Death occurred 3 months after admission, and at autopsy the greatly enlarged liver was found to be studded with small white nodules of growth In the upper lobe of the left lung, which was very hard, a small abscess was discovered On section of the lung a hard white mass was found near the hilum, and spreading outwards into the lung substance The regional lymph nodes were enlarged and hard The histological appearances were said to be those of sarcoma (It is conceivable that this might have been regarded in the present day as an oat-celled carcinoma)

Bennett's case (loc cit) appears more convincing—a woman of 47 with severe dyspnoea, due to a large sanguineous effusion in the right pleural cavity, which aspiration of the fluid failed to relieve The patient eventually died after a profuse haemoptysis A month before death a small secondary nodule was found in the skin at the junction of the 5th right costal cartilage with the sternum This was removed for microscopic section, which revealed a deeply pigmented round-celled sarcoma No general post mortem examination was permitted in this case

Rosenblum and Gasul, reviewing the literature, confirm the general view that primary sarcoma of the lung is an extremely rare condition They record a clear case in a female child aged 2½, which was brought to hospital on account of cough with signs of bronchitis on examination the whole of the right side of the chest was immobile and absolutely dull, breath-sounds and vocal fremitus being absent After death a huge sarcomatous mass was found

vascular, muscular, or meningeal' After this comprehensive description he goes on to insist that it is quite reasonable—if somewhat contrary to general custom—to include the leukaemias, various types of lymphogranuloma (Hodgkin's disease), plasma cell tumours, and malignant tumours of serosal and vascular endothelium in the same category, since they have a common origin in mesenchymal tissues and are prone to exhibit a general similarity of behaviour He further points out that many of the less differentiated sarcomata may, so far as their microscopic characters are concerned, be indistinguishable from other anaplastic forms of growth, and that they may be and often are, exactly imitated by portions of atypical carcinomata The designation of a tumour as malignant or non-malignant depends not solely upon the microscopic characters of its component cells, &c, but also upon *the evidence, histological and clinical, of its behaviour in regard to the rest* of the body We have already seen this in the case of some of those growths described in earlier chapters as benign Moreover, it must always be remembered that *there are varying degrees of malignancy and that* no hard and fast line of distinction is possible in every case

The point of this last observation may be better appreciated after re consideration of three cases in particular among those already described as examples of benign tumours

1 The histological examination of the circumscribed mass, diagnosed clinically as a dermoid (Chap III, Fig 30, p 36), showed a fibro cellular structure which might well have brought it within Willis s definition of a sarcoma The death of this patient, be it noted, was ultimately due to the spread of a bronchial carcinoma discovered accidentally at the operation and apparently quite independent of the circumscribed *tumour in the medi* astinum, to which it bore no histological similarity

2 The supposed neuro-fibroma (Chap IV, p 47, case 4) removed without *undue difficulty by the surgeon*, was subsequently described as a 'fibro sarcoma' by the histologist, who thought it in all probability a growth of 'low-grade malignancy' In this case also death occurred from a quite independent source, a gastric carcinoma, no symptoms referable to the chest having appeared in the interval

3 The xanthoma (Chap V, p 63), quoted by Tudor Edwards (1927, loc cit, case 7), the specimen of which was lodged in the museum of the Royal College of Surgeons, was published by the author as a '*fibro lipo* sarcoma' of the costovertebral angle There seems to have been little or no doubt of the innocency of this tumour in the ordinary sense of the word, recovery after *operation being uneventful, and subsequent* X ray examination some months later showing a perfectly normal chest In all these three cases the growths were evidently mesoblastic in origin

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filling the right side of the chest, the tumour infiltrating the pericardial sac Microscopic examination of sections of the main growth showed it to be a sarcoma In the course of the autopsy they noted hyperaemia and oedema of the left lung, left haemothorax, focal necrosis of the liver, subacute splenitis, swelling of parenchymatous organs, acute and chronic diffuse glomerulo nephritis, multiple infarcts of the kidneys

Endotheliomata In all standard works on pathology and in most of the literature relating to tumours of the lung and pleura reference is made to the endotheliomata It is true that there are vascular connective tissue tumours of the lung which do not fall into the category of well differentiated mesodermal growths and which have been designated 'endotheliomata' It is also true that so called endotheliomatous tumours have been described which appear prima facie to have originated in the pleura and later to have involved the lung, which is found to be studded with more or less discrete nodules of growth similar in character to the main mass Although I am not mainly concerned with questions of histological controversy, there has been so much disagreement among various authorities as to the real nature and origin of these tumours, and so much doubt has been expressed as to whether in fact an endothelioma has any real existence as a pathological entity, that I feel that some attempt must be made to clarify the position

The uncertainty to which I have just referred as to the meaning of this term is reflected in the somewhat cautious observations of modern pathological writers MacCallum, speaking of various growths appearing in some unusual site, and unlike any well recognized tissue, says

> The stumbling block is that a name has been discovered under which all these difficult tumours can be conveniently classified *and thus pigeon-holed and thus withdrawn from further study* [my italics] Every unusual tumour which lacks characteristics that will permit of its ready recognition stands an excellent chance of being labelled an endothelioma and relegated to oblivion There is no reason that endothelial tumours should not arise from the endothelium of the lymphatics or blood-capillaries No doubt they do and possibly some of the tumours described as endotheliomata really have this origin but it is far from proven or even plausible in most cases and in many the essential cells of the tumour though flattened and stretched out are easily shown to be epithelial cells

He goes on to mention primary pleural or peritoneal tumours which can be distinguished from those which occur as metastatic deposits from primary growths situated elsewhere, and while recognizing as do the clinicians tumours of the pleura which appear as a thick white layer of dense tissue covering the lung (*vide* Fig 97, p 152) notes that these contain in the meshes of the connective tissue 'simple or very complicated arrangements of the cells whose nature cannot be positively stated from a study of their mor phology'

Harvey, Dawson, and Innes give a somewhat elaborate classification of the endotheliomata which they define as mesodermal tumours resembling in some of their behaviour the growths of fibroblastic and haemoblastic tissues, and they divide them broadly into the 'vaso-formative', indicating the vascular type of development, and the 'membrano formative', indicating the serosal or synovial type of development The benign types they designate 'endothelio-cytomata', the malignant types 'endothelioblastomata', the latter including the malignant varieties [sic] of the benign forms, as well as the reticulum-cell sarcoma

From all the conflicting views on this difficult question it is not easy for the clinician to arrive at a simple and practical conclusion in regard to this type of intrathoracic neoplasms, which do not conform to any of the more clearly differentiated varieties that have been discussed in the earlier chapters of this work A good deal of light is thrown upon the nature of these growths by Willis's observations on endothelium, which term he applies to the flat layer of cells lining vascular and serous cavities, to which, he says, some histologists would add the layers of cells lining meningeal and synovial cavities He makes a point that it is evident both from embryological and from pathological studies that these flat layers of cells are endothelial 'not by any specific properties of the cells, but by virtue of their positions' and he insists that 'the special properties of endothelial cells of all kinds are, in fact, properties acquired by mesenchymal cells placed in certain positions with respect to special body fluids or other environmental factors ' For this reason he regards the term endothelioma (as ordinarily used) as unnecessary and 'in view of what we know of the plasticity of multiplying mesenchymal cells, inappropriate '

Clinical and Radiological Features. There are, of course, no distinctive clinical manifestations characteristic of mesodermal intrathoracic malignant growths in the chest as often as not the onset of symptoms is insidious, and the clinico-radiological picture does not admit of a definite diagnosis The problem presented to the clinician may be illustrated by reference to the following cases which are appropriately included in one group, the pathology of which I have broadly considered in the foregoing paragraphs

Fig 82 is a radiogram from a boy aged 5 in whom a diagnosis of lymphosarcoma was made This patient was seen in the out-patient department with a swelling over the lower part of the left leg he subsequently developed other swellings in various parts of the body, e g on the left side of the neck, on the back, and on both thighs On admission to the Royal Cancer Hospital in August 1947 he had greatly enlarged lymph-nodes on both sides of the neck and in both axillae The widening of the mediastinal shadow is obvious in the radiogram, which also shows diffuse mottling of both lung-fields, probably

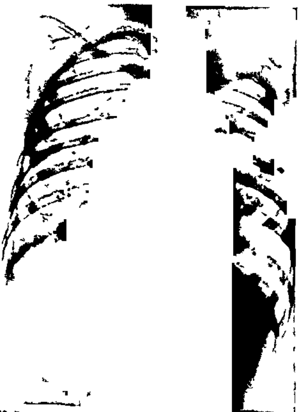


Fig 82 Radiogram of a child with lympho-sarcoma of the lung (By courtesy of Dr Neville Oswald)



Fig 83 Radiogram from a case of lymphadenoma which underwent sarcomatous degeneration (By courtesy of Dr Neville Oswald)

due to deposits in the lymphoid tissue No treatment was attempted in this case, as the parents were loth to keep the child in hospital, and he was accordingly discharged home

Fig 83 is from another patient, a young subject, showing multiple rounded deposits in both lung fields and involvement of the hilar lymph-nodes Similar deposits in this case were found in the subcutaneous tissue, in the colon, and in the liver

The clinical picture of a malignant intrathoracic growth of mesodermal origin is well shown by the following case A boy aged 5 was admitted to the wards of the Miller General Hospital in March 1929 in considerable respiratory distress, pale and anaemic, and with a feeling of constriction in the chest There was a large area of dullness extending to the right and left of the sternum and into the left axilla Râles were heard at both bases The chest was explored with a needle and syringe on the left side and about 3 c c of blood stained fluid was withdrawn which on culture was found to be sterile

The general blood picture was as follows

Total red cells	3 950 000
Haemoglobin	78%
Colour index	1 0
Total white cells	7 600
Differential count	
Polymorphonuclears	74%
Large mononuclears	6%
Lymphocytes	19%
Eosinophies	1 %

The Wasserman reaction was negative

Films of the sputum showed streptococci and staphylococci no elastic fibres, and no cells resembling tumour-cells were seen

X ray examination was carried out on April 9th On the screen a dense shadow could be seen which appeared to overlie the heart shadow and to involve both lungs Viewed laterally the opacity seemed to be more in front than behind No pulsation was observed I regret that the original blocks and films of the radiograms of this case are no longer in existence Figs 84 and 85 are from tracings made of the first reproductions (cf Davidson, *Cancer of the Lung* pp 164 and 165, Figs 60 and 62)

It was concluded that the opacity was due to the presence of a large neoplasm situated in the anterior mediastinum and invading the lungs, chiefly on the left side There was an enlarged cervical lymph node on the right side, but although it was desired to remove this for microscopic section for diagnostic purposes the child s general condition was so bad, and the paracentesis

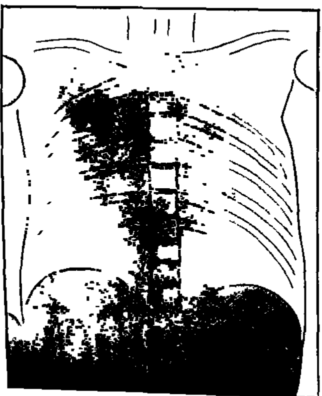


FIG 84 Diagram of radiogram from a case of sarcoma of thymus

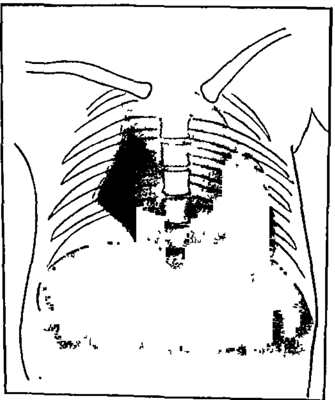


FIG 85 Same case as FIG 83, after treatment with deep X rays

of the chest had frightened and distressed him so much, that it was felt to be undesirable to perform even this slight operation under local anaesthesia

Clinically the diagnosis appeared to rest between that of a primary mediastinal tumour, probably sarcomatous, and that of lymphadenoma involving the mediastinal lymph nodes It was felt that X-ray therapy offered some hope of relief from the distressing symptoms, and despite his serious condition the child was transferred to Guy's Hospital where deep X-ray treatment

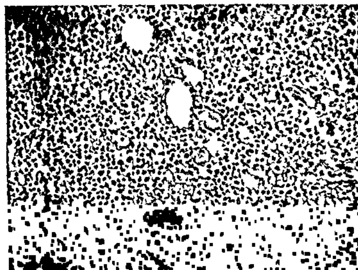


FIG 86 Microphotograph same case as Fig 84 Showing histological appearances of lymph node affected by growth

was given Three days after the treatment had begun there was a considerable clinical improvement dyspnoea being almost absent and the general condition being very much better He was given 6 treatments altogether and the improvement was maintained The area of dullness was markedly diminished as also was the opacity shown in the radiograms On May 13th it was possible to remove the gland from the neck Histological examination of this showed that the normal gland structure was largely replaced by a round-celled sarcomatous growth (Fig 86)

Later on the boy developed a tender swelling over the glabella nothing abnormal could be detected in a skiagram of the skull On May 30th purpuric spots appeared on the abdomen and on the left ankle, and he began to get attacks of epistaxis On June 1st severe melaena and vomiting of dark blood occurred No further purpura developed, but a nodular swelling was observed

in the region of the splenic flexure, and also a tumour in the region of the right kidney The child's general condition was by this time very weak and he showed an extreme 'waxy' pallor Death took place on June 9th

Post mortem. The body was extremely pale, and all the tissues appeared anaemic on section Thorax—the thymus gland was enlarged and firm, it was very hard in the upper part There was a small amount of fluid in both pleural cavities Abdomen—the spleen was slightly enlarged Both kidneys were enlarged, very pale, and covered with sub capsular haemorrhages there were haemorrhages along the lines of the tubules on section The thoracic viscera and portions of the spleen and of the splenic flexure of the colon were removed for microscopic examination This showed appearances similar to those seen in the section of the cervical gland (Fig 86)

The picture presented by the so-called endotheliomata is somewhat different from the above Edwards and Taylor in 1938 recorded a series of 4 cases of primary lung tumours, believed to be of endothelial origin, in which removal by lobectomy was successfully achieved, recovery being uneventful, neither recurrence nor metastasis resulting in any of the cases Three of these patients had complained of cough, which, however, was not severe Expectoration was not a symptom, apart from an attack of haemoptysis in one case Three of the patients complained of discomfort in the chest or upper abdomen, and only one of them of acute pain In this series, then, there was no sudden or dramatic onset of gross symptoms, nor did the patients present a picture of desperate illness The radiograms in all these cases indicated the presence of an intra-pulmonary tumour, the shadow being clearly defined and demarcated from the surrounding lung tissue The possibility of carcinoma had to be considered prior to operation, but the histological reports on the tumours made it clear that they were not malignant, the pathological diagnosis being 'vascular endothelioma' These authors were unable to find any exactly comparable cases in the literature

A good example of what has hitherto been designated an endothelioma of the pleura is given by the following case A young woman aged 26 was admitted to the National Heart Hospital on account of tachycardia, but soon after admission was found to have a large pleural effusion on the right side Her symptoms had begun insidiously, with some pain in the right chest, some weeks before I was asked to see her at the Heart Hospital, and performed a gas-replacement in order to relieve her dyspnoea, which was becoming urgent She was shortly afterwards transferred to Brompton for further observation She then had marked pleural friction in the upper zone of the chest on the right side, there was marked dullness with absence of breath-sounds, vocal fremitus, and vocal resonance at the right base X-ray examination showed appearances indicative of gross pleural involvement with some

residual fluid there was coarse infiltration of both lung-fields which was thought to be strongly suggestive of carcinomatosis The general blood picture was as follows

Total red cells	5 491 000
Haemoglobin	90%
Colour index	0 82
Total white cells	8,200
Differential count	
Polymorphonuclears	83%
Large lymphocytes	4%
Small lymphocytes	3%
Transitionals	9%
Basophils	1%

The pleural fluid was sterile, the cells in it being mainly leucocytes Injection of the fluid into a guinea-pig gave a negative result

Later this patient began to complain of constant dry cough Her dyspnoea increased, she became gradually weaker, and eventually died 41 days after admission

Post-mortem. The right pleura was adherent over the whole lung Below and behind, corresponding to the base of the lung and between the layers of pleura, was a mass of new growth about 3 by 1 inches, whitish in colour, tough in consistence, and showing no signs of breaking down The whole of the right lung was studded with nodules of growth like peas, concentrated mostly in the portion of lung adherent to the main mass of growth (? lymphatic spread) (*vide* Fig 87) The left lung was also infiltrated with similar nodules much less numerous The histological report on this growth was that it showed the appearances of an endothelioma

A somewhat comparable case is recorded by Robertson (1924) in an article on Pleural Endothelioma This was a woman of 57 who had on several occasions had sanguineous fluid aspirated from the right pleural cavity, the clinical diagnosis being a primary tumour of the right pleura At the autopsy on this case the pleural cavity was found to be lined by a whitish layer of soft growth, from 1 cm to 1 5 cm in thickness The lung was collapsed but was not markedly invaded by growth, but metastatic deposits were found in the spleen, the kidney the liver, the left adrenal, and in the mediastinal lymph-nodes, as well as along the course of the aorta Microscopic examination is reported in this paper to have revealed a typical adeno-carcinoma with a tendency to branching papillary outgrowths but the diagnosis at the time of the examination was malignant tumour of the right pleura, probably lymph-endothelioma'

The author's comment on this case is especially interesting He remarks,

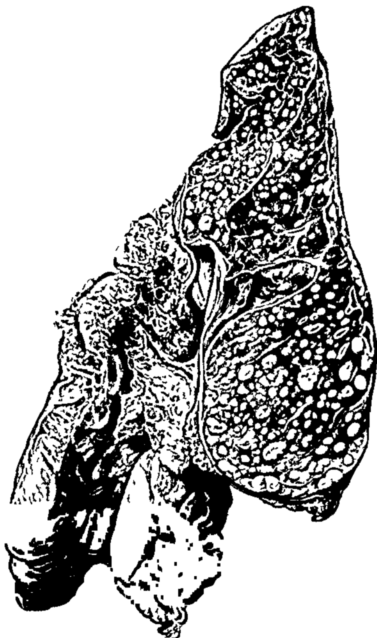


FIG 87 Macroscopic appearances in case of so-called primary pleural endothelioma, with discrete nodules of growth in the lung (Drawing of specimen in the Brompton Hospital Museum) (From Davidson's *Practical Manual of Diseases of the Chest*)

'Except for the rather soft consistency of the pleural portion of the tumour, (tumours of this class usually having a dense fibrous character), the case as a primary malignant tumour of the pleura is fully as acceptable as the majority of those which have been published Whether it would be called a carcinoma or an endothelioma or some other related term *would depend wholly on the personal predilection of the author*' [my italics]

In connexion with the above account it is of interest also to note the comments of Barrett and Elkington (1938) on 2 cases of endothelioma of the pleura, both of which were characterized by marked, progressive, and diffuse thickening of the pleural membrane, with little evidence of actual lung involvement but in which there was a diaphragmatic immobility on one side, and also wasting and paralysis of some of the intercostal muscles on the same side from involvement of segmental nerves by new growth In one of these cases the histological diagnosis was 'fibro-sarcoma', in the other 'a fibro-sarcomatous type of endothelioma' In their introductory observations these authors remark on the lack of general agreement amongst authorities as to the existence of pleural endothelioma as a pathological or a clinical entity In their two cases there was no evidence after careful post-mortem examination of any primary tumour in the bronchial tree, nor of lymphatic invasion, though the new growths were very extensive

Fig 88 is here reproduced not only as an example of a malignant growth which comes into this category but also an instance of the problem of differential diagnosis from the radiological standpoint This radiogram was taken from a woman of 41 who suffered from a long illness which began insidiously with an unexplained pyrexia The interpretation of the abnormal shadows in the radiogram was an occasion for much discussion, some of the suggested explanations being secondary deposits of new growth in the lungs, hydatid disease, and pleural endothelioma An exploratory thoracotomy on this patient revealed multiple tumours growing from the parietal pleura and pressing into the surface of the lung These varied in size from a pin's head to 3 by 2 by 1½ inches Several were removed by diathermy dissection and the sections of these were described as consisting of 'spheroidal eosinophile epitheloid cells, with vesicular nuclei, in places attempting to form tubules, and elsewhere having a whorled squamoid appearance' The conclusion reached was that the appearances were compatible with an endothelioma and that the growth must have been a primary endothelioma of the pleura No growth was found post-mortem in any of the other viscera

The full details of this case have recently been published by Buxton and Willcox (loc cit) I am indebted to the courtesy of Dr Arthur Willcox for a precis of the notes, which he kindly sent me, prior to publication

Yet another similar condition is shown in Figs 89 and 90, which shows

multiple rounded opacities throughout the right lung, with a small effusion at the base This is from a young woman aged 36, who consulted her doctor on account of pain in the right side of the chest, general lassitude, and a feeling of fulness behind the sternum She had been X-rayed first in December 1944,

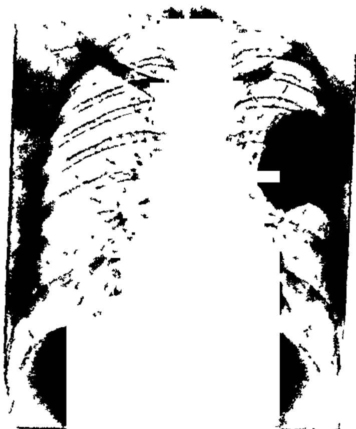


FIG 88 Radiogram from a case of intrathoracic growth diagnosed as a pleural endothelioma (By courtesy of Dr Arthur Willcox and of Dr Campbell Golding)

when she was thought to have pulmonary tuberculosis, and was sent to a sanatorium, where an attempt was made to induce an artificial pneumothorax in April 1945 A little later an enlarged lymph gland was discovered above the right clavicle the pneumothorax therapy was then discontinued and the patient was transferred to Brompton for further observation and diagnosis The supraclavicular lymph-node was removed for biopsy and the following report was received from the histologists

The normal structure of the lymph gland is completely replaced by tumour in this

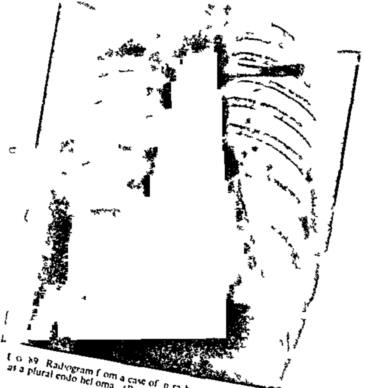


Fig 89 Radiogram from a case of intrathoracic growth diagnosed as a plural endothelioma (By courtesy of Dr J Clifford Hoyle)



Fig 90 Same case as Fig 89 right lateral view (By courtesy of Dr J Clifford Hoyle)

biopsy material There is an area of central degeneration in the larger gland The tumour cells are large, with large vesicular nuclei and prominent nucleoli The cytoplasm is plentiful and deeply eosinophilic The tumour cells in the centre of the gland are growing in a solid mass, but at the periphery they tend to grow in concentric rings as if lining a cavity The general appearance is strongly suggestive of endothelioma

This patient was given deep X-ray treatment at the Royal Cancer Hospital, with some temporary benefit She died eventually in the early summer of 1946, but there is no record that any autopsy was held

I have endeavoured in the foregoing pages to give a précis of existing knowledge on this difficult subject which will be both comprehensive and unprejudiced It will be realized that the precise nature and pathogenesis of the so-called endotheliomata are still a matter for dispute and that, although the term may in time disappear entirely from pathological nomenclature, it is improbable that the last word has yet been said Robertson, whose commentary I have already quoted, notes the general agreement among most authors in their description of the chief signs and symptoms in cases designated pleural endotheliomata This, he considers, suggests that generally speaking, the same region of the body has been affected, and by a similar process in each case He does not, however, in conclusion, feel that the clinical syndrome gives any real indication of the site of the primary growth, though it is evident that the outstanding feature is gross involvement of the pleural surfaces by a malignant growth

In conclusion it may be said that the problems which I have been considering are well illustrated by the following case, which gave rise to no little discussion, both from the clinical and radiological aspects, as well as from the histological standpoint This patient was a young woman aged 27 who began to suffer from pain in the left side of the chest and later developed a swelling in the upper and inner quadrant of the left breast She was treated with simple domestic remedies for some time until the lump began to increase in size and her doctor then sent her to hospital in the country, whence she was referred to the Royal Cancer Hospital On examination there a lump was found in the left breast, 10 by 8 cm in diameter, hard, fixed to the chest wall but not to the skin no enlarged lymph nodes were felt, either in the supraclavicular fossae or in the axillae the right breast and glandular areas were normal

X-ray examination of the thorax showed the appearances seen in Figs 91 and 92 A large rounded intrathoracic tumour is seen occupying the left middle zone and overlapping the other zones The mass is displacing the heart towards the right In some of the films the 4th left rib was seen to be partially destroyed

The case was referred to the surgical department of the Brompton Hospital



Fig 91 Radiogram from a case of intrathoracic neuroblastoma



Fig 92 Same case as Fig 91, left lateral view

for bronchoscopy This showed that the main stem bronchus on the left side was compressed from before backwards nearly as far as the carina it was considered that operative treatment for removal of the growth was impracticable A course of deep X-ray therapy was begun and continued for a period of 40 days (maximum 6,600 r , minimum 4,400 r)

The resulting diminution in the size of the mass is seen in Figs 93 and 94 The whole of the external tumour disappeared and the 4th rib regenerated Later on the patient developed some bronchial dilatation with obstruction to the left lower bronchus, some fluid appeared in the pleural cavity Her general health remained very fair and, except for slight dyspnoea, she remained free from symptoms for about two years In the summer of 1944 she noticed a slight swelling over one rib On further examination as an out-patient she was found to have a hard fixed swelling over the left side of the chest wall, this was felt through the substance of the breast, which seemed to be fixed to the 6th rib, just below the previously irradiated area There was no sign of recurrence in the treated region She was re-admitted for biopsy and for further treatment

A portion of the growth removed from the tumour showed a malignant neoplasm the morphology of which was atypical and indeterminate The malignant parenchyma consisted of compact masses of ovoid or spheroidal cells having large, deeply staining, non-reticulated nuclei with no visible nucleoli, and relatively scanty granular cytoplasm There was no demonstrable intercellular matrix, but there was an abundant stroma composed of collagenous fibrils, in which ramified blood-vessels and nerves, and which contained a small number of muscle fibres Zones of massive and focal necrosis were present both in the stroma and in the neoplastic parenchyma Various histological diagnoses were considered, it was ultimately reported that *by inference this growth fell into the category of an endothelioma of a serous membrane, viz the pleura*

Further irradiation was carried out, to the right side of the chest, anterior and posterior (maximum 2,900 r , minimum 2,800 r) for 23 days, and to the left chest wall, medial and lateral (maximum 3,400 r , minimum 2,500 r) for 18 days

Not long after this it became evident that she was going downhill She began to get severe pain in one leg and she also had a cold and a bad cough A portable X-ray showed increasing consolidation in the right middle and lower zones of the chest She was now losing weight rapidly, dyspnoea was increasing, and she had become cyanosed Death occurred on January 27th, 1945, the total duration of her illness having been approximately 4 years

Post-mortem. Enlarged glands were present in the cervical and retrosternal regions There was a bilateral pleural effusion The left lung was densely

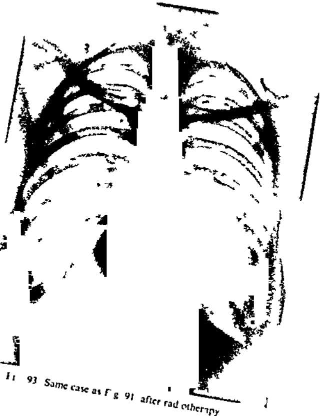


Fig 93 Same case as Fig 91 after radiotherapy



Fig 94 Same case as Fig 93 left lateral view

adherent to the chest wall The right base showed *numerous plaque like* nodules over the pleura and a few *over the middle* and upper lobes *The left* pleura was grossly enlarged and of cartilaginous consistence *The left base* showed a large nodular *growth* extending throughout the lung *parenchyma* The cut surface was whitish, with brown mottling The mediastinal *glands* were infiltrated with *growth, the glands* from the trachea were healthy but the lower part of the trachea and the bronchi were affected The *right heart* was dilated, *there* was some fibrosis of the heart wall, the heart muscle showed some brown atrophy The glandular metastases were white and showed some central softening (Figs 95, 96)

The hollow of the sacrum contained a nodule the size of a walnut extending *from the mid line towards* the right This was extending into the sacral vertebrae, with destruction of bone A segment of the sacrum was removed to show a deposit in the second sacral *vertebra*

The histological report at the time of the autopsy was as follows

> Representative sections from the various viscera involved showed diffuse and extensive malignant infiltration with an anaplastic tumour The tumour parenchyma consisted of *closely packed small* ovoid *cells* having scanty cytoplasm and prominent reticulated nuclei The morphological configuration of this tumour is consistent with a primary endothelioma of the pleura involving in the first instance the lung ribs and chest wall *and subsequently producing metastases in bones lymph nodes and other viscera*

Recently (nearly 5 years later) the specimens from this case have been reviewed and further sections have been cut from the original blocks These were examined by Professor Willis, who was of opinion that the histological appearances were indicative beyond doubt of a *neuroblastoma* which showed in parts typical arrangement of cells in 'rosettes' Though regarding it as impossible from the post mortem findings to be certain of the primary source of the growth he suggested that it might possibly have been the lumbar sympathetic chain, where there was a *tumour mass in the pelvis*

The pathological anatomy of another case of neuroblastoma similar to the foregoing is illustrated in Figs *97* and *98* *These specimens are from a youth*

[illegible]

Aspiration was attempted on two occasions but no fluid was
He was referred to one of the large hospitals in London where further X ray examination showed a large mass occupying the whole of the *left side of the thorax with almost complete* destruction of the 11th rib The liver was enlarged the edge being felt well below the costal margin The large mass of *growth which was expanding* the left chest wall was palpable one hand s breadth into the abdomen It was evident that this mass was increasing *rapidly in size* There was little response to small doses of X rays *The patient s*



Fig 95 Macroscopic appearances in intrathoracic neuroblastoma (From the Pathological Department of the Royal Cancer Hospital by courtesy of Professor R A Willis)



Fig 96 Same case as Fig 95 showing involvement of ribs (From the Pathological Department of the Royal Cancer Hospital, by courtesy of Professor R A Willis)

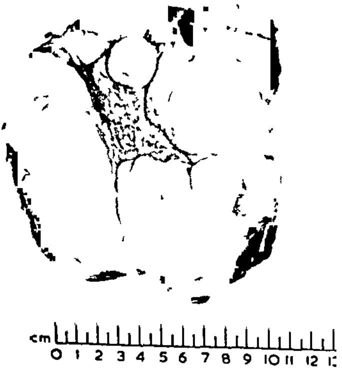


FIG 97 Macroscopic appearances in neuroblastoma (Photograph of specimen from the Museum of the Royal Cancer Hospital by courtesy of Professor R A Willis)



FIG 98 Same case as Fig. 97

general condition was now very bad He was very dyspnoeic on the slightest exertion No treatment had the least effect death occurred about 3 months after he had first reported sick

At autopsy an enormous tumour was found in the chest, presumably arising from the left thoracic chain It filled the left half of the thorax, displacing the diaphragm downwards and involving it at one point It also directly extended to the pectoral muscles through the first intercostal space, and infiltrated the ribs on the left side

Histologically the tumour was found to be a neuroblastoma, with plentiful 'rosette' formation The only metastasis found was in one left axillary lymph node The macroscopic appearances are shown in the two accompanying photographs (Figs 97 and 98)

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XI

SECONDARY MALIGNANT GROWTHS IN THE CHEST

I HAVE previously referred (p 10) to the phenomenon of metastasis as generally characteristic of malignancy and as the chief criterion for the division of tumours into the benign and the malignant varieties Although in this work I have been mainly concerned with primary intrathoracic neoplasms, some reference must be made to the general picture of secondary malignant disease in the lungs, both from the clinical and from the radiological standpoint

I have already indicated that sarcoma of the lung as a primary condition is an extreme rarity, practically all sarcomatous deposits in the chest are secondary to a growth which has originated elsewhere in the body The obvious sarcomata are highly malignant tumours, composed of rapidly growing undifferentiated cells, the supporting stroma being relatively scanty The blood-vessels in these growths are lined by a single layer of endothelium, in many instances this can hardly be differentiated, and the vessels appear as little more than blood spaces between the actual tumour cells which form the only lining For this reason these cells are particularly liable to dissemination by the blood stream to various parts and especially to the lungs A striking example of this is seen in the case of osteogenic sarcoma of the femur, a condition met with most commonly in children and young adults Even after early amputation of the limb the outlook is extremely bad, the appearance of secondary deposits of growth in the lungs and elsewhere may be anticipated, sometimes within a few months, or even weeks, of the discovery of the primary tumour Fig 82 (Chap X), which for purposes of convenient classification has been included in the general account of mesodermal growths, is an example of secondary sarcoma of the lungs and mediastinum The same may be said of the so called pleural endotheliomata, which though appearing in many respects to be primary pleurogenous growths, have lately by various authorities been regarded as metastases from some primary deposit (in the suprarenal body, prostate, or elsewhere) that has escaped detection at the autopsy

In many of the cases described as lympho sarcoma or reticulo sarcoma of the lungs the pulmonary lesions are but one manifestation of a widespread deposit of masses of lymphoid tissue which characterizes a variety of clinical syndromes that have been grouped together under the generic term 'reticuloses', which includes such conditions as reticulo-sarcoma, lympho sarcoma, lymphatic leukaemia, and various forms of lymphogranuloma (Hodgkin s disease) In these it can hardly be maintained that the pulmonary lesions are

primary lung tumours in the ordinary sense of the word, and for this reason I have felt it proper to refer to them in a section of this work which deals with secondary malignant growths of the chest.

The accompanying illustrations (Figs 99 to 103) may be taken as representative of the various radiological appearances seen in patients in whom a primary carcinoma of some organ has given rise to metastatic deposits in the lungs

Diagnosis of the condition is not always obvious from X-ray evidence alone The occurrence of symptoms or signs suggestive of serious intrathoracic disease in a patient known to have had a cancerous lesion of some viscus must necessarily suggest the dissemination of metastatic nodules in the chest, but the clinical picture varies considerably, and, however great the suspicion, confirmation of the presence of secondary carcinoma is by no means always easy Symptoms may, and not infrequently do, arise long before the appearance of any unequivocal evidence in the X-ray picture, and it is seldom, if ever, that physical examination of the chest gives any reliable information Metastatic disease in the lung occurs most commonly in the form of scattered roundish nodules, more or less circumscribed, throughout the lung-fields These may exist in fair number without any gross respiratory disability, since the total functional respiratory area is not greatly diminished and the vital capacity may still be comparatively high An example of this is seen in Fig 99, which shows the X-ray appearances in the chest of a patient who developed secondary deposits in the lung and mediastinal lymph glands from a primary carcinoma in the prostate The density of the shadows and their irregular outline in such a radiogram should always suggest the diagnosis of new growth, but the search for the original focus may often fail to show the site of the primary lesion which may only be discovered post-mortem Even at autopsy the primary focus, if small may easily escape detection A similar appearance is seen in Fig 100 which shows a large oval shadow in the right upper zone There is nothing in this picture that is diagnostic of carcinoma the opacity might easily be attributed to a relatively benign lesion such as a neuro fibroma or other circumscribed tumour Actually this radiogram is from a patient with a large mass of carcinoma which originated from a primary growth in the tonsil He was a man aged 80 who was treated by high-voltage radiotherapy at the Royal Cancer Hospital in the early part of 1943 for carcinoma of the tonsil Later he developed a cough with blood-stained expectoration, and masses of enlarged lymph-nodes appeared in the right axilla Histological examination of biopsy specimens showed bulky metastatic deposits of squamous-celled carcinoma In some of the radiograms of this case the mass in the right upper zone of the chest was seen to have caused destruction of portions of the 2nd and 3rd ribs



FIG 99 Radiogram showing secondary deposits of growth in the lungs from a primary carcinoma of the prostate gland (By courtesy of Dr J Clifford Hoyle)

FIG 100 Radiogram showing a large secondary deposit of growth in the chest from a primary carcinoma of the tonsil (By courtesy of Dr Campbell Golding)



Fig 101 Radiogram showing secondary deposits of carcinoma in the lung in a patient who had an amputation of the breast 5 years previously (From Davidson's *Practical Manual of Diseases of the Chest*)



Fig 102 Radiogram showing secondary carcinomatosis of lungs from a primary growth in the gall bladder (By courtesy of Dr J Clifford Hoyle)



FIG 103 Rad ogram from a case of secondary carcinomatosis of lungs (site of primary *growth unrecorded*)





FIG 104 Radiographic appearances *in lymphangitis* carcinomatosa (primary growth in the stomach) (By courtesy of Dr J Clifford Hoyle)

Figs 101, 102, and 103 illustrate the state of affairs more commonly seen Fig 101 is a radiogram from a patient who had had a Halstead's operation for carcinoma of the breast 5 years previously She was complaining of dry cough and shortness of breath and had been losing weight The X-ray appearances are indicative of widespread dissemination of fairly large deposits



Fig 103 Radiogram showing diffuse miliary carcinomatosis of lungs secondary to a growth in the breast (By courtesy of Dr J Clifford Hoyle *Chronic Miliary Tuberculosis* Hoyle & Vaizey Oxf Univ Press)

of carcinomatous growth throughout the lung fields In Fig 102 the dissemination is even more extensive and the nodules appear coarser this is from a man who had a primary carcinoma of the gall bladder Fig. 103 shows a typical secondary carcinomatosis of the lungs (the primary source here is unrecorded)

The greatest degree of respiratory distress is seen in those cases in which the greater portion of all the lung fields is infiltrated with fine secondary deposits (Assmann's lymphangitis carcinomatosa) Fig 104 shows this condition the primary growth in this case was in the stomach the commonest origin of growths which metastasize in this way The root shadows in such cases are always large and the patient is always much distressed very dyspnoeic and cyanosed The course of the disease at this stage is rapid usually limited to

a few months at most Fig 105 shows a diffuse miliary carcinomatosis of the lungs, secondary to a primary growth in the breast Here the nodulation is diffuse and moderately fine, the appearances simulating some examples of silicosis or of chronic miliary tuberculosis

One of the commonest secondary results of bronchial carcinoma is a malignant pleuritis, due to metastatic deposits of growth in the subpleural region As I have already pointed out (Chap VIII), though pleural effusion is practically always a late phenomenon in the course of the disease, it is occasionally the first clinical manifestation to direct attention to it

XII

MISCELLANEOUS TUMOURS

DIFFERENTIAL DIAGNOSIS

In my introductory remarks (p 1) I indicated that my object was to outline the present position of medicine surgery and radiology in relation to thoracic new growths and to describe various groups of the latter as they present themselves in practice I have so far been concerned with those lesions which can be enumerated under more or less definite headings It remains to deal with certain others which do not fall into any one single pathological category which are not all strictly speaking neoplastic but which from the diagnostic and therapeutic standpoint it is convenient to consider in any general review of this kind

LYMPHADENOMA

The inclusion of lymphadenoma among the intrathoracic new growths seems to be justified by the general behaviour and ultimate clinical manifestations of the thoracic type of this disease The original description by Hodgkin in 1832 referred to a series of cases which exhibited a general enlargement of the lymph nodes with lymphoid deposits in the spleen the aetiology of which was obscure Several of the German authors having noted a certain resemblance of Hodgkin s disease to lymphatic leukaemia were wont to speak of it as pseudo leukaemia but no attempt was then made to connect it systematically with various allied conditions as has been done in recent years under the general heading of diseases of the reticulo-endothelial system In modern nomenclature the so-called lymphadenopathies are sometimes referred to as reticulosis or reticulo-endotheliosis The definition suggested for this group of diseases by Robb-Smith is a progressive hypoplasia of reticular tissue with differentiation to one or more cell types He observes It is commonly systematized that is to say it affects throughout the body tissue homologous to that affected in the lymph node Further free cellular elements may be present in the circulating blood (leukaemia) The following classification based on Robb-Smith s work is given by Beattie and Dickson and enables one to link up the various manifestations of this great group and to appreciate their relationship to the different clinical syndromes

Reference to Tables XX and XXI will make clearer the connexion between primary blood diseases such as the leukaemias and some of the intrathoracic neoplasms described in Chapter X as well as their relation to the lymphadenomatous conditions of which the classical Hodgkin s disease is the example

TABLE XX *Classification of the Reticuloses*
(Beattie and Dickson)

	The Reticuloses
Medullary	[illegible]
Primary	[illegible]
Metabolic (the generalized lipoidoses)	[illegible]
Primary	[illegible]
Follicular	[illegible]
Sinus	Primary; Infective

I would also quote the classification given by these authors of the reticulo-sarcomata

TABLE XXI *Classification of the Reticulo sarcomata*
(Beattie and Dickson)

	Reticulo sarcomata
Undifferentiated	Diffuse Trabecular
Differentiation to histoid cells	Fibrillo-syncytial Fibrillary
Differentiation to haemic cells	Lymphoblastic Lymphocytic (lympho-sarcoma) Myeloblastic and myelocytic (myelomatosis &c) Plasmocytic Erythroblastic
Mixed type	Polymorphic reticulo sarcoma
Differentiation to sinus lining cells	Undifferentiated cell type (reticulo-endothelio-sarcoma) Differentiated type (histiocytoma)

generally recognized by the clinician The case illustrated by Fig 83, p 136, for example, and described as a reticulo sarcoma, originated as a case of Hodgkin's disease [sic] in which the condition subsequently underwent sarcomatous degeneration The causation of lymphadenoma is still obscure, nor have we any real explanation of its clinical variations It is of some interest to note that, so far as my experience goes, in those cases which exhibit the well known syndrome of gross enlargement of cervical and axillary glands with splenomegaly one does not see a corresponding affection of glands in the mediastinum Conversely the cases of obvious intrathoracic lymphadenoma which come to the chest specialist seldom show any gross or extensive enlargement of glands in the neck or axillae

Clinical and Radiological Features. In most instances the patient with mediastinal lymphadenoma seeks advice for symptoms referable to the chest, *e g* cough, and occasionally some pain which is commonly in the second or third intercostal space to one or other side of the sternum There may be a



FIG 106 Radiogram from a case of Hodgkin s disease (By courtesy of Dr Campbell Golding)

history of malaise and debility, but quite often the general health appears to be unaffected Dullness to percussion may be present to the right or left of the sternum, according to the extent of glandular enlargement in the chest, and there may be some alteration in the character of the breath-sounds if there is pressure on a bronchus X-ray examination, even at an early stage of the disease, may show some widening of the mediastinal shadow, some partial collapse of a lobe, or possibly an actual tumour As the disease progresses, the physical signs become more obvious, and the abnormal X-ray shadows,

TABLE XX *Classification of the Reticuloses*
(Beattie and Dickson)

	The Reticuloses
Medullary Primary	[illegible]
Metabolic (the generalized lipoidoses) Primary	Gaucher s disease Niemann Pick s disease Xanthomatosis (including lymphogranuloma inguinale and regional ileitis (Crohn s disease))
Follicular	Lymphoid (follicular lymphoblastoma) Fibrillary
Sinus	Primary Infective

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history of malaise and debility, but quite often the general health appears to be unaffected Dullness to percussion may be present to the right or left of the sternum, according to the extent of glandular enlargement in the chest, and there may be some alteration in the character of the breath-sounds if there is pressure on a bronchus X-ray examination, even at an early stage of the disease, may show some widening of the mediastinal shadow, some partial collapse of a lobe, or possibly an actual tumour As the disease progresses, the physical signs become more obvious, and the abnormal X-ray shadows,

which at first are often unilateral, extend to both sides of the chest. Although, as I have said, gross involvement of the cervical and axillary glands is uncommon in these cases, a single enlarged lymph-node, or perhaps two, may be found, usually above one clavicle, sometimes in the axilla, and when the radiological diagnosis is still in doubt, the matter may be settled by histological examination of the gland, which can often be excised without undue difficulty under a local anaesthetic, though occasionally it is deeper seated, when removal may involve a more prolonged operation.

Fig. 106 gives a fairly representative picture of the X-ray appearances in a typical case. This patient had actually sought advice in the first instance on account of swelling in the neck and swelling of the right arm which she had noticed for some months. Her weight had been constant and she had had no cough or respiratory discomfort, but X-ray examination of her chest prior to radiotherapy showed a small opacity above the right clavicle. Biopsy of a lymph node from the right axilla showed appearances typical of Hodgkin's disease, viz. loss of structure, with endothelial overgrowth, giant cell formation, and eosinophilic infiltration. Treatment by deep X-rays was given on two occasions, with an interval of 11 months, after which she remained in good general health and without symptoms for some years. Eventually she returned to hospital complaining of dyspnoea on exertion and slight cough. She was then found to have some prominence of the chest-wall over the sternum and in the second right intercostal space. Some enlarged glands were present in the left supraclavicular fossa. The diagnosis in this case had been established histologically from the start; from the radiological appearances alone, however (Fig. 106), it would hardly be possible to be dogmatic about the nature of the mass at the right hilum. This appears fairly well circumscribed; the relative opacity of the surrounding lung field, as compared with that on the left side, suggests lymphatic stasis from pressure, or possibly even infiltration. Apart from the history and the histological evidence already obtained, and judging the radiogram by itself, a diagnosis of primary bronchial carcinoma might not unreasonably have been considered.

Figs. 107 and 108 are radiograms taken from another patient at an interval of 21 months. Each shows a state of affairs not uncommon in mediastinal lymphadenoma. In the earlier one there is collapse and consolidation of the right upper lobe, the appearances being very similar to those frequently produced by a carcinoma of the right upper lobe bronchus. In the later picture the lung has again become aerated, but widespread infiltration of the glands is apparent, both upper and middle mediastinal groups being affected as well as the broncho-pulmonary glands on the right side.

Differential Diagnosis. If in a case of mediastinal lymphadenoma there are accessible cervical or axillary glands which can be removed for biopsy,

Fig 107 Radiogram from a case of Hodgkin's disease showing collapse of right upper lobe owing to bronchial obstruction from pressure of enlarged lymph nodes (By courtesy of Dr Neville Oswald)

Fig 108 Same case as Fig 107 showing enlargement of three groups of glands in Hodgkin's disease (By courtesy of Dr Neville Oswald)

diagnosis of the condition may be a comparatively easy matter Otherwise, diagnosis is often impossible from the X-ray picture alone The radiogram shown in Fig 106, for example, is, as I have pointed out, practically indistinguishable from that of many cases of collapse of the upper lobe due to pressure on the bronchus by a carcinoma Opacities in the upper part of the



Fig 109 Radiogram from a case of hydat d disease of the lung (By courtesy of Dr Campbell Golding)

mediastinum due to lympho sarcoma, to a thymoma, or to the lymphoid deposits of the leukaemias may bear a close resemblance to those of Hodgkin's disease Although in most established cases the radiological shadows in the latter are bilateral, this is not invariable, and unilateral glandular enlargement may simulate a tumour of quite different character, e g a teratoma, or even a hydatid cyst In cases of doubt, the radiotherapeutic test may decide the point, not infrequently a diagnostic application of X-rays is advisable when lymphadenoma or some allied condition is suspected but unaccompanied by histological evidence

HYDATID DISEASE

Simple bronchial and alveolar cysts do not as a rule give rise to much difficulty in differential diagnosis, but hydatid cysts within the chest vary a good deal as regards their radiological appearances, and may not infrequently be mistaken for solid tumours It is for this reason that I have felt that some reference to them, with illustrative examples, would not be inappropriate in a work on intrathoracic new growths In Chapter IV I cited an example of a large extra pulmonary tumour which was removed surgically and found to be a neuro-fibroma In this case the radiologist reported that the presence of a fibroma should be considered 'if an encysted effusion *or a hydatid* were thought to be clinically unlikely' (cf Fig 33, p 41) It will be of interest to note in comparison with this the X-ray appearances in Fig 109, which is a radiogram from a case of hydatid disease of the lung These two postero-anterior views are by no means dissimilar, and give some idea of the difficulty in differential diagnosis which not infrequently arises Yet another example is afforded by Figs 110 and 111 which show a mass of considerable size in the right middle zone, seen in the lateral view to be lying anteriorly From these radiograms alone a positive diagnosis would seem hardly possible The nature of the lesion in this case was established prior to operation by examination of the fluid from the cyst obtained by aspiration, this showed the presence of hooklets and scolices It may be observed at this point that the only unequivocal pre-operative evidence of hydatid disease in the chest is the discovery of hydatid elements in some pathological fluid associated with the tumour The complement fixation test, applied by Ghedini in 1906 to the diagnosis of hydatid disease, is a group reaction, not specific (other antigens, *e g extract of taenia saginata, extract of fasciola hepatica, or fluid from* cysticercus tenuicollis, have been used in lieu of hydatid fluid) This test has apparently given better results on the whole than the precipitin test, investigated by Fleig and Lisbonne in 1907 This was carried out by incubating a mixture of 0 5 c c of hydatid fluid with 0 5 c c of the patient's serum in a test tube for 2 hours at a temperature of 37 C a precipitate being given in positive cases The Casoni test, first described in 1911, appears to be the most reliable of any Intradermal injection of 0 2 c c of sterile hydatid fluid obtained from the cysts of sheep, pigs, oxen, or humans with injection of 0 2 c c of saline as a control, gives an immediate local reaction in positive cases Accompanying the local reaction is an erythematous wheal, which increases in size and reaches its maximum within 10 to 30 minutes The observations of Lemaire and Thiodet in 1926 showed 17 per cent of positive reactions with the precipitin reaction, 17 per cent with the complement fixation test, and 87 per cent with the Casoni intradermal test

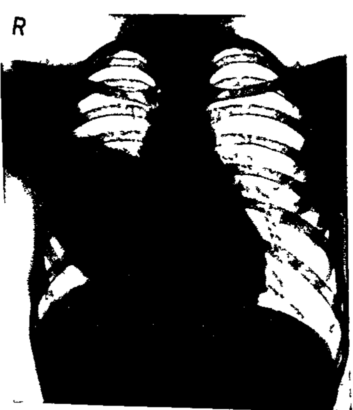


Fig 110 Rad ogram from a case of h dat d d sease of the lung (From Dav dson s *Pract cal Ma ual of D seases of tl e Chest*)



Fig 111 Same case as Fig 110 r ght lat ral v e v

Fig. 112 is a diagram from a case recorded some years ago (loc cit) of a young man whose medical history had been rather misleading, the story of cough and expectoration, dyspepsia, and haemoptysis, subsequent to an attack of left-sided pleurisy 18 months previously, being strongly suggestive of pulmonary tuberculosis The X-ray appearances are indicative of a very

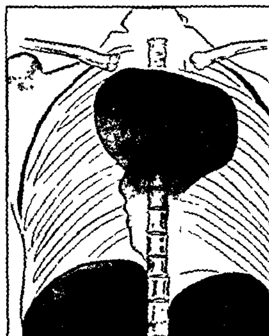


Fig 112 Diagram of radiogram from a case of hydatid cyst of the mediastinum (From Davidson's *Cancer of the Lung and Other Intrathoracic Tumours*)

large tumour in the upper part of the chest, almost identical with those in some cases of solid benign tumours (cf Fig 15) This actually proved at an autopsy to be a large hydatid cyst, containing numerous daughter cysts This patient had at a late stage of his illness developed a compression paraplegia, presumed at the time to be due to tuberculous caries of the spine No exploratory operation or laminectomy had been permitted by the relatives

ANEURYSM OF THE AORTA

The recognition of an aortic aneurysm may not, perhaps, be regarded as an outstanding problem in differential diagnosis, but cases do occur in which there may be initial difficulty in distinguishing it from other intrathoracic

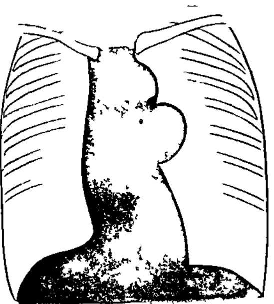


Fig 113 Diagram of radiogram from a case of aortic aneurysm

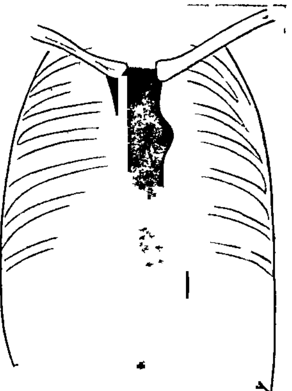


Fig 114 Diagram of radiogram from a normal chest, for comparison with Fig 113



FIG. 115 Radiogram from a case of aortic aneurysm (By courtesy of Dr Campbell Golding.)



FIG. 116 Radiogram showing aortic aneurysm (By courtesy of Dr. G. Simon.)

tumours The pressure symptoms caused by an aneurysm are similar to those resulting from any large mediastinal growth and in any case in which a radiogram shows a shadow in the mediastinum consistent with aneurysm the possible presence of a neoplastic tumour is not necessarily excluded by the fact that the patient happens to exhibit a positive Wasserman or Kahn



FIG 117 Kymogram Same case as Fig 116 (By courtesy of Dr G Simon)

reaction Both the X ray appearances and the physical signs in lymphadenoma may resemble those in some cases of aneurysm from which moreover it may sometimes be difficult to distinguish an intrathoracic goitre

In suspected cases in which the clinical evidence is insufficient to establish a definite diagnosis the radiological examination must be very complete in order to determine the relation of the abnormal mediastinal shadow to the aorta Right and left anterior oblique views will frequently make this sufficiently clear but sometimes it is desirable to resort to kymography or even angiography The kymograph may be invaluable in determining whether

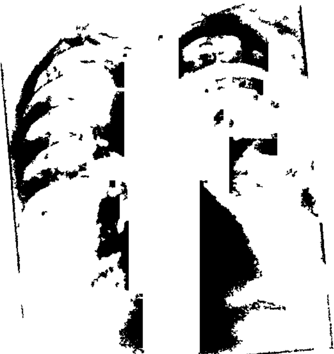


Fig. 118 Radiogram of media nal umour (By courtesy of Dr G. S mon)





Fig. 119 Kymogram Same case as Fig 118 (By courtesy of Dr G. S mon)

or not there is expansile pulsation in the tumour, for upon this point may depend the differential diagnosis between an aneurysm and a mediastinal new growth or a mass of lymphadenomatous glands Even the kymograph however, is not an infallible guide, a remarkable case having been recorded by Fiske and Grace of a man aged 34 with a typical brassy cough, dyspnoea and occasional pain in the region of the right shoulder This patient exhibited clinically some pulsation in the suprasternal notch, and dullness with slight pulsation over the upper part of the sternum, a little to the right of the aortic area The Wasserman reaction was strongly positive The radiological examination, which included kymography, showed a large opacity, about 4 inches in diameter, above the aorta, the aortic arch being displaced to the left The kymogram, contrary to expectation, showed no pulsation in the mass, which was apparently immobile The radiological examination was repeated on two further occasions, the reports being identical with the first and on the strength of the absence of pulsation the authors performed an exploratory thoracotomy in the hope that they might discover an operable mediastinal tumour What was actually found, however, was a saccular aneurysm, springing from the arch of the aorta and filled with blood clot

INTRATHORACIC GOITRE

A substernal goitre may be recognizable from a typical X ray picture, which shows a more or less triangular shadow with the base uppermost and the apex below This is, however, by no means invariable the opacity being sometimes unilateral and occasionally circular, so that the appearances may suggest either a lobar collapse or a mediastinal tumour The latter is most likely to be simulated by a very large and unilateral intrathoracic thyroid as the following illustrations show

These radiograms are taken from a case of intrathoracic goitre in a man aged 68 Fig 120, a postero anterior view, exemplifies the problem of differential diagnosis from the radiologist s point of view when compared for example, with a postero anterior radiogram of a known case of neurofibroma (cf Fig 37, p 44) or again with one of a teratoma (cf Fig 20, p 29) In this case no detailed diagnosis was made on the ordinary postero anterior and lateral films by the radiologists, who reported a large tumour, with a sharp lateral edge, in the upper and middle zones on the right side Fig 123 shows the state of affairs after induction of a diagnostic pneumothorax which makes it clear that the mass is extra pulmonary

The clinical history of this patient is as follows His symptoms which began in the spring of 1942, were pain in the right side of the neck, especially when his head was turned to the left He was treated for this with short wave diathermy without effect Early in 1943 he was examined by another doctor



Fig. 120. Radiogram from a case of intrathoracic goitre



Fig. 121. Same case as Fig. 120



FIG 122 Same case as Fig 120 (lateral view)





FIG 123 Same case as Fig 120 (after induction of diagnostic pneumothorax)

who made an X-ray examination which disclosed the presence of the tumour. There was nothing of significance in the past medical history. The man had lost weight (about a stone and a half) in the preceding 6 months, he had recently complained of slight cough in the mornings, but was not unduly breathless Physical examination revealed some dullness in the upper part of the chest to the right of the sternum, where the respiratory murmur was inaudible The cardiovascular system appeared normal, the blood-pressure readings were 110 *mm* (systolic), 70 *mm* (diastolic) The vital capacity was 1,800 c c

An exploratory thoracotomy was carried out (posterior approach, resection of the 6th rib and the posterior segment of the 5th rib) The right lung was found to be free The upper part of the chest was occupied by a large, round, smooth tumour, stony hard in places, and fluctuating at the lower pole It was not adherent to the lung It arose from the upper part of the mediastinum by a pedicle of moderately firm tissue The pleura was incised and the tumour mobilized by stripping the pleural membrane from the line of reflection on to the growth It now became apparent that the pedicle consisted of normal thyroid tissue coming from the region of the trachea Some of the larger veins of the pedicle were exposed by blunt dissection, the remainder being cut and tied There was considerable bleeding from the side of the tumour, the tissues being very friable After removal of the tumour the cut ends of the pleura were sutured together so as to cover the exposed mediastinal structures, an opening being left at the bottom for drainage The chest was closed and the patient left the theatre in good condition Recovery was uneventful, and the patient was discharged from hospital 4 weeks later

Pathological examination showed the mass to consist of apparently normal thyroid tissue The report was as follows 'Thyroid gland showing a fair degree of fibrosis The alveoli are rather irregular in size, some contain normal looking colloid, others are empty, some appear hyaline Most of the cells lining them are flattened There is recent haemorrhage in many areas

I have quoted the above case to show the difficulty which may occasionally arise in distinguishing a goitre of this type from a benign tumour of the lung or mediastinum It seems to have been a genuine instance of the intrathoracic goitre proper as distinct from the substernal goitre The latter includes the so-called mediastinal goitre, in which 'the intrathoracic mass arises from the isthmus or from one of the lateral lobes and comes to lie in the mediastinal space medial to the great vessels and in front of the aorta' (Joll)

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XIII

RADIOTHERAPY

By D W SMITHERS, M D , M R C P , D M R

1. Introduction

THE use of ionizing radiations in the treatment of patients with tumours has been in progress now for 50 years, but the regular accurate application of a prescribed dose to a selected volume of accessible tissue containing the tumour, with a fairly clear idea of what may be expected to follow such treatment, is comparatively recent A corresponding stage in the development of radiotherapy for patients with deep-seated tumours has not yet been reached for a number of reasons, some clinical and some technical The results of treatment by radiation of patients with carcinomas of the tongue, or cervix uteri, are good, while the results with tumours of similar structure in the oesophagus, or bronchi, are bad The difference is due partly to the fact that accessible tumours are more often and more easily detected at an early stage, partly to the more accurate assessment of size and spread of the accessible tumour, which allows localization of the treatment to the tissues involved, and partly to the fact that the radiation does not have to pass through the normal tissues to reach the tumour Radiation is a most effective means of treating patients with malignant tumours of certain histological structure provided that its effect can be localized to the tumour, that little damage is done to the normal tissues, and that the whole tumour is adequately irradiated When radiotherapy is used under unfavourable conditions for tumours whose exact dimensions situation, and spread are unknown, and which are completely surrounded by normal tissues, its beneficial effects are greatly diminished, and it is only effective in special cases where a number of unusual circumstances chance to be in its favour This usually means the presence of a highly active but still localized tumour in a fit patient

Radiotherapy does not produce direct destruction of all tumour cells, its use is in no way comparable to cauterization Massive doses outside the range used therapeutically will produce tissue necrosis by direct destruction, and much smaller therapeutic doses if given to areas previously heavily irradiated [illegible]

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radiation) come into action, and the growth of the tumour may be controlled for a time or the whole tumour may be eliminated If such cells are scarce and evenly distributed, no such general tumour disorganization occurs, the normal tissues do not receive the same chance of dealing with the growth of the part over which they have lost control, and the tumour is said to be *radio-resistant*

The difficulties presented to the radiotherapist by thoracic tumours are all too clear such tumours are inaccessible, often deeply situated, ill defined, and difficult to localize their individual degree and direction of spread are speculative and not all of them are of favourable histological structure The patients are often elderly, frequently ill, and sometimes wasted Results of treatment can only be improved by using every aid towards accurate estimation of the volume occupied by the tumour, by localization of the radiation effect to this volume, and by the reduction of the irradiation of the normal tissues to a minimum, thus obtaining the most favourable distribution of dose with time so as to get the best effect possible with the particular histological type of tumour present, and promoting the patient's own general resistance which is so helpful in producing a successful result with radiation therapy With many intrathoracic tumours there is no inherent reason why they should not respond well to irradiation, the reasons that they do not do so more often are that with present treatment methods the normal tissues around are damaged almost as much as the tumours, that only part of the tumour may be affected at all, that we do not know enough about the general histological structure in each case from examination of the small pieces usually obtained for biopsy, and that, if we did, our knowledge of radio-biology is still inadequate to enable us to plan the most suitable individual dose-time distribution, moreover, the patients are so often too ill or the disease process too widespread for any effective treatment to be attempted Though the difficulties are great there are a number of ways in which some of them can be overcome and some grounds for believing that irradiation of the tumour, combined with a general rise in the patient's resistance, offers the best hope known to us at present of improving the survival rate in the large number of patients who develop malignant intrathoracic neoplasms

2. Carcinoma of the Bronchus

An attempt will be made here to set the individual treatment problem presented by a patient with a carcinoma of the [illegible] with all the diffi-
culties that have just been [illegible] ainst the b[illegible] of the incidence
of the disease and to ass[illegible] value [illegible] both as a
palliative, and as a possible [illegible] ure in [illegible] other methods
of treatment available Ti[illegible] to [illegible] of the diffi-

culties enumerated above will be described and plans for the future discussed The results of treatment in a group of cases and the details of the method employed will be given in full

The Treatment Problem

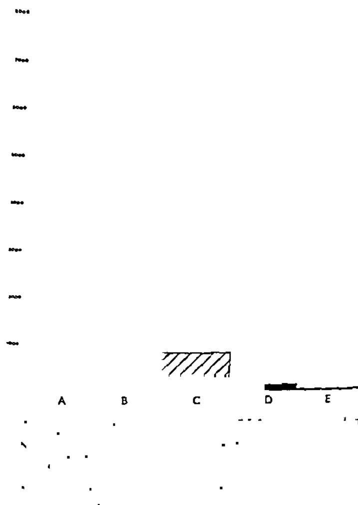
In Chapter VI the present incidence of carcinoma of the bronchus has been discussed and an indication given of the magnitude of the treatment problem with which we are confronted At the present time there are thought to be between 8 000 and 9,000 deaths per annum in England and Wales attributable to bronchial carcinoma There are good reasons for thinking that the higher figure is nearer to the true annual mortality The number of these patients receiving treatment was estimated by MacKenzie (1939) at only 5 per cent of the total incidence, this figure has certainly increased but is still low Tod (1949) in her inquiry into the extent to which patients with cancer in Great Britain receive radiotherapy included lung tumours in a group with others treated by radiation for palliation but for which surgery is usually preferred in suitable cases The average proportion treated in this group was found to be 25 per cent

The percentage treated by radiotherapy of the cases registered at Bradford were however, given for the lung as 13 and a table was included which suggested that this was fairly representative of the British Isles as a whole She estimated that 50 per cent of the patients developing carcinoma of the lung required radiotherapy Fig 124 is an estimate made (Smithers 1949) of the treatment position for bronchial carcinoma in this country in 1945 in an attempt to show how insignificant our present effort to deal with this disease still is and that there is scope for any method of treatment that has any pretensions to deal effectively with even a small proportion of the total cases seen Such considerations should place any reports claiming a few successes, such as that to be presented below in their proper perspective, they apply at least as forcibly to the results of surgical or chemical as to those of radiation treatment

The position, then, is that in this country some 9 000 persons develop bronchial carcinoma annually, of which perhaps no more than 2 per cent have a pneumonectomy or lobectomy which are generally regarded as the only hope of cure Little more than 10 per cent have other forms of treatment which hold out any prospect of producing temporary arrest of tumour growth, and in only 4 per cent is treatment other than surgical given which is even planned to attempt more than this This means that at the moment attempts to cure these patients are only being made in about 6 cases in every 100

CARCINOMA OF THE BRONCHUS

Estimate of number of cases per annum in England and Wales Number treated and number surviving five years. (Based on figures for 1945)



mate)

D Number treated by surgery estimated at 150 (15 per cent of all cases treated) excluding exploration without removal (May be overestimate)

E Number surviving five years estimated at 25 cases (2 5 per cent of all cases treated) (Probably an overestimate)

FIG 124

(With acknowledgements to the Annals of the Royal College of Surgeons of England, *1949, Vol IV)*

An Analysis of 500 cases of bronchial carcinoma

If we consider the larger treatment centres fully staffed and equipped for thoracic surgery and radiotherapy, the position, though changed, is still a serious one. Although a considerably greater proportion of the patients seen are treated, most of this treatment is still only palliative. Of 500 consecutive patients with carcinoma of the bronchus seen at the joint clinic for neoplastic diseases held by the Brompton Hospital for Diseases of the Chest and the Royal Cancer Hospital 123 (24.6 per cent.) were unfit for any treatment, in 178 (35.6 per cent.) some palliative X-ray therapy for relief of symptoms was given, in 57 (11.4 per cent.) advanced cases an attempt at palliation was made with chemotherapy, and in 142 (28.4 per cent.) some attempt at radical treatment was made even though the disease was already advanced with signs of extensive lymph node invasion in some cases. That is, the disease in over 70 per cent. of the patients seen was so advanced that no treatment making any pretence to effect a cure could be tried. The cases referred to this clinic are, of course, selected, as some of the best and some of the worst of those seen at the two hospitals are not referred to the clinic, the best being operated on and the worst being so bad that it was thought to be unjustifiable to send them on to the joint clinic for further consideration. It is not possible as yet to give the accurate total figure from which these were selected, as the records of the patients who did not attend the clinic have not been reviewed, and some were not fully investigated. The diagnosis of carcinoma of the bronchus was, however, recorded in another 442 patients from 1944–8 who were not seen at the consultation clinic. Table XXII shows the distribution of the 500 cases seen according to the treatment given. Although most patients operated on are not referred to the clinic, every patient seen has been reconsidered from the point of view of operability and 9 were in fact operated on. Four patients thought to have operable tumours but without confirmation by means of thoracotomy received radical X-ray therapy because they refused operation.

TABLE XXII

Pneumonectomy	9	Operation 18	Radical treatment 142 (28%)
Pneumonectomy and post-operative X rays	7		
Pneumonectomy with pre-operative X rays and chemotherapy	1		
Pneumonectomy and chemotherapy	1		
Radical course of X ray therapy	107	Radical radiation 124	
X ray therapy and chemotherapy	17		
Palliative X ray therapy	178	Palliative treatment 235	No attempt at cure 358 (72%)
Chemotherapy	57		
Not treated	123		

Thirty three patients had a thoracotomy without removal of the tumour and these have been classified as not treated if nothing further was done or placed in the appropriate group if treatment was then given.

It can be seen from Table XXII that 310 patients were treated with X-rays In 7 the treatment was given after operation either because it was thought that the risk of recurrence in the mediastinum was high or because it was clear at the time of operation that invaded lymph-nodes remained behind Six of these patients have died 13, 12, 10, 11, 6, and 4 months after their treatment, and one is still alive and well 22 months after treatment One hundred and seventy-eight received palliative treatment amounting in some cases only to a fe v small doses for relief of pain due to secondary deposits or to test radiosensitivity, but in most cases to an attempt to relieve the patient of distressing symptoms Seventeen were treated experimentally by a combina tion of X-rays and chemotherapy (10 with chloro-ethylamine, 6 with urethane and 1 with urethane and dienoestrol), 11 died within the first year, 5 in the second year, and 1 (treated with X-rays and chloro ethylamine) is alive 2 years and 3 months after treatment One hundred and eight received a radical course of X-ray therapy (including 1 who had a subsequent pneumonec tomy) The distinction between palliative and radical irradiation is usually quite clear, in some of the palliative cases no attempt to treat the primary tumour was made at all, and in most the treatment was stopped as soon as relief of the symptoms for which the treatment was given was obtained There is a small borderline group, however, in which the original intention was simply the relief of some symptom, but where the initial response was good enough to persuade us that treatment should be persisted in in the hope not only of relieving distress but also of prolonging life Whenever these patients have received a tumour dose of 4,000 r or more they have been arbitrarily counted as having had a radical treatment Similarly patients who started on a planned course of radical treatment, but who for one reason or another were unable to complete it and received a tumour dose of less than 4 000 r, have been classed as having had palliative treatment only This dose of 4 000 r, arbitrarily chosen, is well below the planned tumour dose in most cases and was chosen so as to bias the selection in the borderline group in favour of radical rather than palliative treatment A few patients having palliative treatment lived for more than 1 year, but none for more than 2 All patients lost sight of (20) are regarded as having died of cancer within the first year No deaths from 'intercurrent disease' have been counted as such all have been attributed to cancer, and no cases have been omitted The records of the whole 500 patients have been recently reviewed, those of all patients living more than 1 year have been reviewed in detail, including re-examination of radiograms, and, where available, of histological sections The diagnosis of carcinoma of the bronchus was rejected in 47 of the patients referred in the same period, so that the 500 cases analysed were taken from 547 sent for consideration of treatment Three were rejected, despite the fact

that they originally had positive pathological reports, on the grounds that they remained well, one for 6 years, and review of the sections suggested that there was insufficient evidence firmly to support the original diagnosis

The results of treatment are presented in Tables XXIII, XXIV and XXV divided into those with histological confirmation of the diagnosis and those without who have been accepted after review by physician, surgeon, and radiotherapist at a consultation clinic as having good clinical evidence to support the diagnosis Throughout the worst and not the best possible results

TABLE XXIII *Survival of 500 Consecutive Patients with Carcinoma of the Bronchus seen at the Brompton Hospital and Royal Cancer Hospital Joint Consultation Clinic from May 1944 to December 1948*

Year	No seen	With histological confirmation A	Without histological confirmation B	Number alive at the end of: 1 yr A	1 yr B	2 yrs A	2 yrs B	3 yrs A	3 yrs B	4 yrs A	4 yrs B	5 yrs A	5 yrs B
1944	79	43	39	15	6	5	3	1	0	1	0	1	0
1945	107	62	45	19	14	3	3	2	0	0	0		
1946	118	75	42	15	13	7	1	3	1				
1947	105	70	35	14	7	4	3						
1948	91	59	31	8	3								
Total	500	307	193	71	43	19	10	6	1	1	0	1	0
Number surviving				114		29		7		1		1	
Absolute survival rate				22 4%		6 6%		2 3%					

TABLE XXIV *Results of Treatment by X-ray Therapy in Inoperable Cases of Carcinoma of the Bronchus With (A) and Without (B) Histological Confirmation of the Diagnosis*

Year	No seen	Not treated A	Not treated B	Treated other means A	Treated other means B	Treated X rays only A	Treated X rays only B	Number treated by X-rays only alive at the end of: 1 yr A	1 yr B	2 yrs A	2 yrs B	3 yrs A	3 yrs B	4 yrs A	4 yrs B	5 yrs A	5 yrs B
1944	79	9	12	2	0	29	27	12	6	4	3	1	0	1	0	1	0
1945	107	8	18	16	6	38	21	13	9	1	2	1	0	0	0		
1946	118	18	14	10	0	48	28	13	12	5	1	2	1				
1947	105	15	9	32	6	23	20	4	5	2	3						
1948	91	13	10	20	1	26	21	3	2								
Total	500	63	63	80	13	164	117	45	34	12	9	4	1	1	0	1	0
Total		219				281		79		21		5		1		1	
Absolute survival rate of those treated by X rays								28 1%		9 4%		2 6%					

TABLE XXV *Results of Treatment by Radical X-ray Therapy in Inoperable Cases of Carcinoma of the Bronchus*

Year	No seen	Palliative X ray therapy		Radical X ray therapy		Number treated by X rays only alive at the end of									
						1 yr		2 yrs		3 yrs		4 yrs		5 yrs	
		A	B	A	B	A	B	A	B	A	B	A	B	A	B
1944	79	18	21	11	6	8	1	2	0	1	0	1	0	1	0
1945	107	26	12	12	9	5	7	1	2	1	0	0	0		
1946	118	30	17	18	11	10	7	5	1	2	1				
1947	105	12	13	11	7	3	3	2	1						
1948	91	8	16	18	5	3	1								
Total	500	94	79	70	38	29	19	10	4	4	1	1	0	1	0
Total		176		109		48		14		5		1		1	
Absolute survival rate of inoperable cases treated by radical X ray therapy						45 0%		17 6%		7 5%					

that could be claimed from the records kept have been presented Figs 125, 126, and 127 show the radiograms before and after treatment of the patient who survived longest in this group

The records of the patients treated from 1938 to 1944 (Table XXVI) are not so complete or so accurate as those of the 500 cases presented above There were, however, two who lived for more than 5 years following radio therapy One, a man of 65 treated in May 1939, died 7 years later in April 1946 We were unable to obtain any particulars except that his death certificate stated that he died from metastases from carcinoma of the lung The other, a man of 58, was treated in September 1940 and is still alive and well in

TABLE XXVI *Results of X ray Treatment for Patients with Carcinoma of the Bronchus seen in the Radiotherapy Department of the Royal Cancer Hospital from 1938 to May 1944*

Year	Number of patients seen	Number of patients treated	Number confirmed histo logically	Untraced	Died under 1 year	Died 1 to 2 years	Died 2 to 3 years	Died 3 to 4 years	Lived for 5 years or more
1938	21	20	14	2	15	4	0	0	0
1939	28	25	23	0	24	2	0	1	1*
1940	19	19	13	1	15	2	0	0	1†
1941	14	13	8	0	12	2	0	0	0
1942	24	22	12	1	21	0	1	1	0
1943	20	20	12	0	17	3	0	0	0
1944	7	6	4	0	4	1	2	0	0
Total	133	125	86	4	108	14	3	2	2

* Died 7 years after first treatment
† Still alive 9 years after first treatment

January 1950, 9 years later This man was bronchoscoped at the London Chest Hospital in 1940 when a carcinoma of the right main bronchus just below the bifurcation of the upper lobe bronchus was seen, and a piece removed for biopsy showed squamous-cell carcinoma The block and slides were lost in an air-raid and it has been impossible for us to confirm this diagnosis In 1944 he was re-bronchoscoped and the right upper lobe orifice was found to be narrowed but no tumour was seen The X-rays of his chest now show some fibrosis in the treated area on the right side

Some of the published results of treatment of patients with bronchial carcinoma can be seen in Table XXVII which is abstracted from a paper by

TABLE XXVII *Results of Treatment of Carcinoma of the Bronchus by X-rays*

Abstracted from Leddy Radiology 1943

Author	*Number of patients seen*	*Number of patients treated*	*Number confirmed histologically*	*Died under 1 year*	*Alive 2 to 5 years*	*Alive 4 years or more*	*Remarks*
Saupe 1936		200	67	140 (70%)	0	0	None lived more than 2 years
Kerman, 1936		104		100 (96%)	0	0	4 lived 15 28 months
Vinson 1936	140	84			at least 8	less than 6	8 lived 4 years or more 6 lived 4 7½ years
Tchaperoff 1937		46			at least 6		6 alive 4 years after treatment
Schinz and Zuppinger 1937		69		68 (99%)	0	0	1 lived more than 15 months Average 4 4 months
Engels 1938		92	36	72 (78%)	2	1	1 alive 3 years 1 alive 5 years average survival 11 5 months
Craver 1940	175	142		137 (96%)	5	1	2 lived 4½ years 1 lived 12½ years
Farberov and Barlow 1941		*6	44		7	0	6 lived 15 months to 3 years average 8 months
Leddy and Moersch 1940	250	125	125	100 (80%)		5	Half not treated as control All died in 1 year 1 treated lived 12 years

Leddy (1943) and in Table XXVIII which has been compiled from some more recent publications It is, however, difficult to judge the value of radio therapy from such tables, as they tell us nothing about relief of symptoms, they leave us wondering if the few isolated successes ever did have carcinoma of the bronchus, considering the ease with which mistakes can be made, and they represent in most cases a type of treatment ill adapted to the purpose of localizing the energy absorbed to the tumour, and so only calculated to produce some degree of palliation

TABLE XXVIII *Results of Treatment of Carcinoma of the Bronchus by X-rays*

Author	*Number of patients seen*	*Number of patients treated*	*Number confirmed histo logically*	*Number died under 1 year*	*Number alive 2-5 years*	*Number alive over 5 years*	*Remarks*
Flood, 1943	*70*		*44*	*54*	*1*	0	
Dobbie 1944		170	50	156 (92%)	4	2	1 alive 5 years 1 at 6 years
Widmann 1944	286	167		149 (89%)	5	2	1 alive at 6 years
Hilton 1945	179	93	92	66 (71%)	8	0	2 alive over 4 years
Shorvon 1947	*213*	*138*	*79*		3	0	No histological confirmation in the 3 survivors

Treatment policy

Even though surgery deals most effectively with the few operable cases of bronchial carcinoma, it is clear that at present it only touches the fringe of the treatment problem and that it is unlikely to improve its position greatly without either a revolution in diagnosis or by combination with some other form of treatment Chemotherapy, as is shown in Chapter IX, has so far proved to be of no value in the treatment of bronchial tumours and has often caused considerable added distress to some of the patients so treated Radio therapy tackles a larger section of the problem than surgery but tackles it less efficiently Nevertheless, after the few most favourable cases have been removed, it still provides hope of some years' survival to a few and great temporary benefit to many, despite the grave disadvantages, which were discussed in the introduction to this chapter, under which it still labours as a treatment method for such patients At present it reduces tumour activity, relieves symptoms, and prolongs life in many cases, see Figs 125 to 131, but produces complete tumour regression in few We are anxious to know how best to take advantage of what it offers now and how to overcome some of the many difficulties so that we may improve the prospect for the future



Fig 1'5



Fig 1 6

Figs 125 1 6 and 1'7 A manufacturer aged 64 who coughed up a p ece of anaplas c carcinoma more than 1 cm in d ameter At broncho-scopy the growth was seen n the pectoral branch of the right upper lobe bronchus and the X rays showed a rap dly grow ng mass w th collapse of the pectoral segment Treated w h X rays No ember 1944 Al e well and symptom free f ve years later

Figs 125 and 1'6 Before treatment

It would seem to be clear from the knowledge that we have at present that we should continue to advise operation for all suitable cases When there is doubt as to the advisability of operation, where, for instance, the activity of the tumour is known to be unusually high, radiotherapy should be given

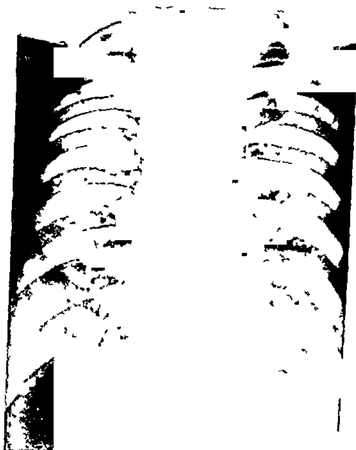


FIG 127 Seven months after treatment

with the idea that some of these patients will become suitable for operation at a later date This group is likely to be small Only one is contained in the series of 500 referred to above, but one other has since been treated in this way and more post radiation pneumonectomies have now been planned The next group of patients have inoperable tumours but no clinical evidence of widespread dissemination, and are in fairly good general health, these are mostly suitable for a carefully planned course of radical X ray therapy A few patients in poor general condition, or with gross superadded infection can be treated first with rest, diet, and penicillin until they improve enough for



Fig 128 Before treatment

Fig 129 Three months later

Figs 128 and 1 9 A chauffeur aged 50 w th carc noma of the left upper lobe bronchus and a h lar mass and a left vocal chord paralys s, who following X ray treatment lost h s cough and dyspnoea but cont nued to t re eas ly he was otherwise well and ga n ng we ght 6 months later

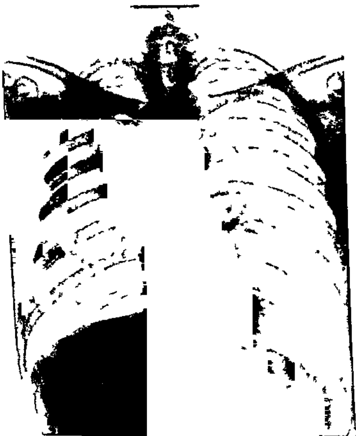


Fig 130 Before treatment

Fig 131 After treatment

Figs 130 and 131 A pastry cook male aged 33 w th a carc noma of the r ght upp r lobe bronchus found at thoracotomy to have a mass of nvaded med ast nal nodes inoperable Pall at ve treatment w th rad otherapy given with good immediate response pat ent remain ng well for 5 years before develop ng symptoms from recurrence

radical treatment Many of the remainder are unfit for any radical treatment, but some have distressing symptoms which may be relieved In general it is wise to obtain this relief as quickly as possible without adding further to the patient's discomfort, and to stop the treatment immediately this is accomplished Prolonged palliative treatments often defeat their own ends Radiotherapy is of chief value as a palliative for the relief of superior vena caval obstruction, haemoptysis, cough, and, less frequently but sometimes quite dramatically, of dyspnoea For pain it is not so satisfactory since, though it commonly relieves the pain due to secondary deposits in bone, it is far less often effective when there has been direct transpleural invasion of bone by the primary tumour The pain caused by some superior sulcus tumours has proved to be particularly resistant to irradiation There does not seem to be any benefit following irradiation of patients with bronchial carcinoma who have developed pleural effusions

Radical X-ray therapy

Radical radiotherapy is reserved for those patients with inoperable tumours who have no signs of extrathoracic spread, no pleural effusion, who are in or can be got into fairly good general condition, and who have not yet developed such a massive primary or secondary growth within the chest that a large volume of tissue would have to be irradiated and an adequate localized tumour dose could not be given Since the only hope of long survival following irradiation is in those cases in which the tumour is confined to a reasonably small volume which can be adequately treated without undue damage to the surrounding tissues, indiscriminate wide field treatment to cover all possible extensions of the disease is on this score doomed to failure If a limited volume presumed to contain the whole tumour is adequately treated some chance of success exists, if the assessment of tumour size and spread was incorrect, nothing is lost in most cases, since no large volume treatment is likely to have been successful The techniques of radical radiotherapy for bronchial carcinoma are, therefore, concerned with localizing the volume to be treated, with keeping this as small as possible and not yielding to a desire to stretch it for safety's sake to cover possible untreatable extensions of the disease, with localizing the high dose to this volume and giving as little as possible to the tissues around, and with attempting to arrange the distribution of dose with time to the best advantage for the type of tumour to be treated There are a number of ways of tackling these problems, those adopted by us have already been described (Steed, O'Connor, Lamerton, Winternitz, Mayneord, and Smithers, 1949) but a review of the main points in the technique employed for the patients said to have had 'radical radiotherapy' in the 500 reviewed above will be given here

From a radiographic examination (usually employing an antero posterior and a lateral view and a series of tomographs), a consideration of the broncho scopic report, and a microscopical examination of any piece removed for biopsy, a decision is taken as to the size and position within the chest of the volume of tissue to be treated It is not possible to irradiate adequately a



FIG 132 Radiogram of the chest of a patient with car

sphere of more than 8 or 9 centimetres in diameter with the apparatus available at present, and then only if the tumour happens to be fairly radio sensitive Once the diameter has been decided and the central point of the volume for treatment fixed (Fig 132), the points on the skin on the front and back of the chest directly over this central point are located Radiograms are taken with the patient in the positions in which he will be treated, supine and prone with his head and shoulders on a special rest (Fig 133) A pointer is used to direct the beam for exposure (Fig 134) and this is placed over the sternal angle anteriorly and over the spine of the 4th dorsal vertebra posteriorly

so as to be directed approximately at the carina in both cases During exposure the pointer is removed and a disc fitted in its place on the diagnostic tube This disc carries a central lead spot which records the position of the chosen skin point on each radiogram (Fig 135) The projection of the volume to be treated is then marked on each film (Fig 136) The films then show the relative positions of the central rays of the beams with which they were taken (lead spot) and the vertical projection of the mid-point of the volume to be treated The distance between these points can be measured on the film with a ruler which corrects for the magnification (Fig 137) As the posi-

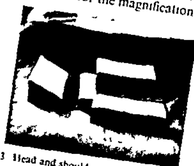


FIG 133 Head and shoulder rest (With acknowledgements to the *Brit Journ Radiol*)

tions of the skin points corresponding to the lead marks are known, the skin points directly overlying the centre of the volume selected for treatment when the patient is in the two treatment positions can be found and marked by tattooing on the skin Centring on these tattoo marks eight evenly spaced radial lines are drawn anteriorly and posteriorly four in one colour and the intermediate four in another (Figs 138 and 139) The skin points overlying the centre of the volume selected for treatment which have been located should lie on a vertical line when the patient is in either treatment position The distance of the centre of the treated volume from the carina (which is often situated at approximately the same level) is measured on each film to see that they correspond, as this acts as a check Angled beams of radiation are then arranged along the radial lines that have been drawn at varying distances from the skin point overlying the centre of the volume to be treated, and at various angles so as to provide cones of radiation intersecting at a depth and leading to a high localized tumour dose (Fig 140) The size of the fields are varied according to the size of the volume to be treated and a special beam-directing device is fitted to the X-ray tube to ensure that the treatment conditions prescribed can be constantly reproduced (Fig 141) Four fields on lines marked in one colour are treated on one day and the four on lines marked in the other colour on the next, alternating with anterior and posterior

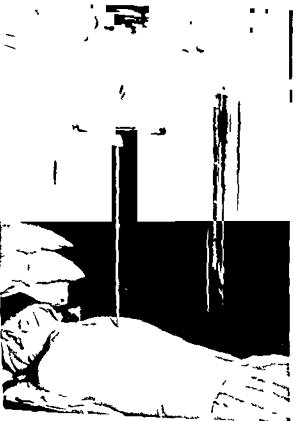


FIG 134 Pointer attached to a cone on the diagnostic X ray apparatus and used to direct the beam when exposures are made for localization (With acknowledgements to the *Brit Journ Radiol*)



FIG 135 Radiogram showing the image of the lead spot on the central ray (With acknowledgements to the *Brit Journ Radiol*)



FIG 136 Circle indicating volume to be treated marked on a transparent film and then superimposed on the rad ogram so that the position of its mid point is recorded (With acknowledgements to the *Brit Jo rn Rad ol*)

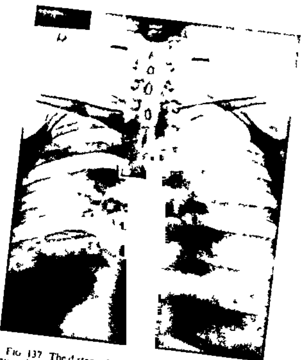


FIG 137 The d stance between the lead spot on the central ray and the project on of the mid point of the volume to be treated is measured on the radiogram (With acknowledgements to the *Brit Journ Rad ol*)

fields By this means the tumour near the apex of a cone of radiation produced by four fields is irradiated daily, but the normal tissues nearer to the skin surface are only irradiated every fourth day The accuracy of the application can be checked at any time by inserting an X ray film under the patient



FIG 138 Slotted Perspex disc centred on the axial skin point and used to mark the radial lines (With acknowledgements to the *Brit Journ Radiol*)

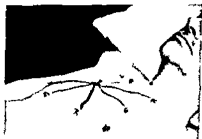
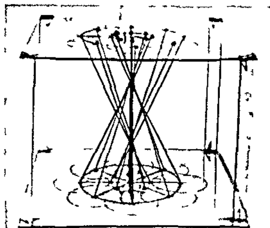


FIG 139 Radial lines marked on the skin four in red (*R*) and four in green (*G*) (With acknowledgements to the *Brit Journ Radiol*)

during treatment so that it is exposed to the four beams of radiation (Fig 142) A diagram is drawn to represent the theoretical pattern of blackening that should be found (Fig 143) and this is compared with that actually produced (Fig 144) By such means, using a 400 kV X ray plant *it is possible* to deliver doses to tumours within the thorax of the order of 300–400 per cent of those given to the skin (Figs *145 and 146*)

Future Plans

Steps are now being taken to carry this treatment further by introducing a method of continuous rotation of the patient during irradiation in place



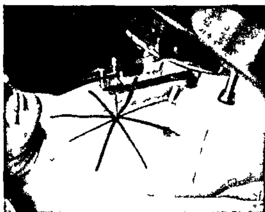


FIG 141 Patient in position for treatment (With acknowledgements to the *Brit Journ Radiol*)

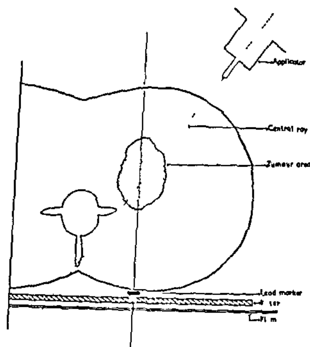


FIG 142 Diagram showing the method of record ng the accuracy of the beam direction during treatment The pattern of the beams on the exit surface is recorded on a film (With acknowledgements to the *Brit Journ Rad ol*)

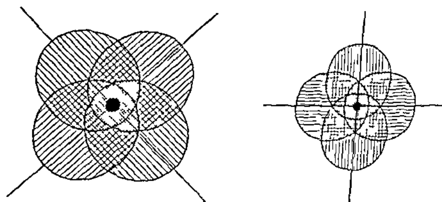


FIG 143 Two examples of the theoretical patterns which should have been produced dur ng treatment by four beams of X rays on films placed on the far side of the patient parallel to the plane of entrance of the beams (With acknowledgements to the *Brit Journ Rad ol*)

of the discontinuous treatment with multiple fields arranged ar)und the circumference of a circle which has been described above This will be used with a 2 million volt X ray therapy plant to start with and poss bly with a 20 million volt synchrotron at a later date Such methods will improve the

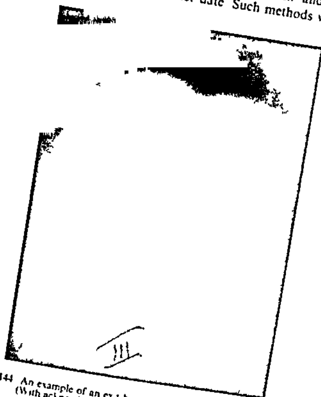


FIG 144 An example of an ex t beam pattern taken during treatment (With acknowledgements to the *B t Journ Ra l ol*)

dose distribution in space and enable us to give a higher more localized tumour dose with less damage to the normal tissues At the same time attempts are being made to improve the dose distribution in time so as to adapt the treatment to the individual tumour This is a more difficult problem depending for progress partly on cytological analysis of particles of tumours removed at different times during a course of treatment partly on special experiments and partly on trial and error While efforts are being made to improve the direct effect of the treatment on the tumour there is also an attempt in progress to increase the patient s resistance and to help the important indirect effects of treatment to play their part

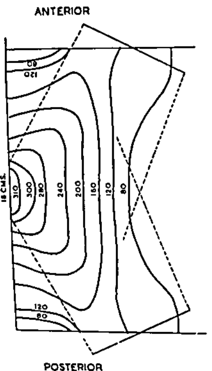


FIG 145 Sixteen field distribution Symmetrical arrangement of fields, 400 kV, 50 cm F S D Eight fields anterior and posterior each 7 cm in diameter at 65 degrees and 8 cm radius Distribution in a plane passing through the centre of any field Maximum skin dose 160 per cent (With acknowledgements to the *Brit Journ Radiol*)

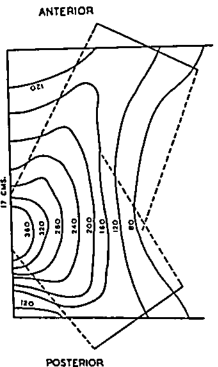


FIG 146 Sixteen field distribution Asymmetrical arrangement of fields, 400 kV, 50 cm F S D Eight fields anterior each 7 cm in diameter at 65 degrees and 9 cm radius Eight fields posterior each 7 cm in diameter at 55 degrees and 8 cm radius Maximum skin dose 170 per cent (With acknowledgements to the *Brit Journ Radiol*)

3. The Lymphatic Tumours

Radiotherapy is the only efficient method of palliative treatment available for most cases of intrathoracic lymphadenopathy or lymphatic tumour. Effective as this treatment frequently is for local manifestations of the disease, it seldom, however, has any real influence on the ultimate outcome, since it does not remove the tendency for similar tissues to be affected throughout the body, nor does it deal effectively with widespread dissemination. In the thorax this group of tumours may involve a variety of structures such as the mediastinal lymph-nodes, thymus, lung, pleura, or bones, and may display a variety of not very clearly distinct histological forms including lympho-sarcoma, lymphadenoma, giant follicular lymphadenopathy, and the leukaemias.

The position with regard to treatment is quite unlike that for carcinoma of the bronchus. Here we are dealing as a rule with highly radiosensitive masses which form part of a generalized disease process. Attempts to deliver high doses to restricted volumes of tissue are quite out of place, and regional treatments with large fields and much lower doses are required to deal with the more obvious manifestations to relieve pressure and toxic reactions and to prepare the way for attempts, as yet purely experimental, to deal more effectively with the underlying fundamental disease process. Irradiation usually takes the form of large field X-ray therapy varying from total body irradiation, which is now seldom employed, to the irradiation of one lymph-node region or of one solitary lesion. The introduction of artificially radio-active isotopes in treatment has however provided a new method of approach to this problem. Isotopes may be used for their chemical affinity for certain tissues or cells in the hope that they will be selectively absorbed in the tumour tissue to an extent which will make treatment by this means feasible, or for their physical properties when given in the form of inert particles which are ingested by phagocytes and localized by physiological processes. Phosphorus[32] is an example of one commonly used in the first group and Colloidal Gold[199] of one in the second.

Since radiotherapy for these cases is only effective on a local or at best a regional basis, attempts are made to combine it with some other form of treatment which it is hoped may affect the fundamental disease process as a whole or may so raise the patient's resistance as to enable him to overcome the disease. These are at present tentative efforts divided into the use of general cytotoxic poisons like the chlorethylamines, which sometimes have a useful temporary effect but which do not seem to prolong life, the use of artificial fever which has not proved satisfactory in practice, despite some interesting regressions noted with intercurrent febrile diseases, and the

attempt to raise the patient's general resistance by dietetic and hormone therapy On this basis radiotherapy is directed to removing large masses causing pressure symptoms or other embarrassment, to reducing the toxic effects of the disease, and to putting the patient in the best possible position to take advantage of any more general treatment method which is on trial or which may appear It is also of value in some cases as a therapeutic test in helping to establish the diagnosis

The intrathoracic lesions seen with the lymphatic tumours may appear in a variety of forms In general the localized lymph-node enlargements respond best to radiotherapy both on a short and on a longer term basis The small group of cases of lymphadenoma, with mediastinal lymph node enlargement as the only sign of the disease when first treated, usually respond well and have a comparatively good prognosis Patients with widespread nodular infiltration of the lung parenchyma tend to respond much less well, and those with generalized lymphangitic dissemination less well still Unfortunately the response of these cases to chlorethylamines, though occasionally satisfactory for a while, seems to be of brief duration The most rewarding cases from the point of view of radiotherapy are those with predominantly lymphoid hyperplasia, the giant follicular lymphadenopathies, or the lymphoid follicular reticuloses This condition is of importance because it has a tendency to give rise to pleural effusion, sometimes bilateral, so that the patient may be regarded as too ill or as having too advanced a condition to warrant treatment With radiotherapy, however, the effusions frequently absorb and the patients may return to full health for as much as 5 to 10 years, an outcome which is not seen with lymphadenoma

The treatment to be given to these patients must clearly be decided quite separately for each individual No special technique with individual variations such as that employed for carcinoma of the bronchus would be appropriate The extent of the X-ray fields used, the dose, the use of radioactive phosphorus or colloids, the associated methods of more general treatment will all depend on the symptoms, degree and type of dissemination, histology, and general condition and outlook of the patient

The use of radiotherapy as a diagnostic test is practically confined to cases with mediastinal lymph node enlargement of unknown cause where there are no specific changes in the peripheral blood or bone marrow, and no accessible node which can be removed for biopsy If a dose of 1,000–1,500 r is given to the mediastinal nodes, in 10–14 days they are likely to show marked regression within the first month from starting the treatment if the enlargement is due to one of the radiosensitive lymphadenopathies (Figs 147 and 148) If the enlargement is due to sarcoidosis the response is likely to be similar to that seen with lymphadenoma but will not normally be noted for

Fig 147 Before treatment aged 20 Nodes regressed rapidly

Fig 148 After treatment

Figs 147 and 148 Girl of 16 treated with X rays to enlarged lymph nodes in neck due to Hodgkin's disease Well for four years Mediastinal mass treated with X rays at the age of 20 well for another 4 years then developed generalized lymph node enlargement and died aged 25



FIG 149 Before treatment

FIG 150 Two years later

FIGS 149 and 150 Girl aged 19 with enlargement of nodes in neck and mediastinum due to *sarcoidosis* Sanatorium treatment for 6 months without effect Treated by X rays with slow but good regression of lymph node mass

approximately two months (Figs 149 and 150) If it is due to secondary deposits from primary carcinoma arising in the bronchus or elsewhere no very obvious response is likely to be noted with such doses at any rate during the first two weeks though with oat cell carcinomas of the bronchus some regression may be seen at times with doses of this order within 1 month of starting treatment

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XIV

OPERATIVE TREATMENT OF THORACIC NEW GROWTHS

By O S TUBBS, M A, M B, F R C S

FROM the surgeon's point of view thoracic neoplasms may be divided into two main groups (1) Broncho pulmonary neoplasms, that is those occurring within the lung or bronchial tree, and (2) those arising from the structures forming the mediastinum and chest wall

It is usually easy to decide from clinical and radiological evidence to which group any individual patient belongs, but, in cases of difficulty, further investigation by bronchography or by the induction of an artificial pneumo thorax may be required to settle the point

BRONCHO-PULMONARY NEOPLASMS

The surgical treatment of broncho pulmonary neoplasms will be considered according to their pathological nature, although some tumours of differing histology, particularly certain rare innocent neoplasms, are grouped together The following classification has proved convenient and rational

1 Innocent' Tumours
   - (*a*) Adenomata
   - (*b*) Papillomata
   - (*c*) Chondromata
     Hamartomata
     Osteomata
     Fibromata
   - (*d*) Haemangiomata
   - (*e*) Teratomata and Dermoid Cysts

2 Malignant Tumours
   - (*a*) Bronchial Carcinomata
   - (*b*) Sarcomata
   - (*c*) Metastatic growths

The adjective 'innocent' is employed by tradition to tumours which do not form metastases, haematogenous or lymphatic, and it is used here in that sense Even so, there are some authorities who would not agree to the adeno mata being labelled 'innocent', because these tumours not uncommonly show malignant characteristics sooner or later, and for this reason it has been suggested that it would be preferable to consider them as adeno carcinomata of low grade malignancy However as the surgical treatment of a typical adenoma may differ considerably from that of a typical adeno carcinoma it is considered justifiable to include the adenomata with the 'innocent' growths

ADENOMATA

As these tumours occur in the large bronchi, it is possible in the great majority of cases to remove a piece of the tumour by means of bronchoscopy so that the exact nature of the growth may be known when planning treatment. The adenomata are frequently very vascular and the bronchoscopist must therefore be prepared for quite a brisk haemorrhage following the use of the biopsy forceps on a tumour suspected of being an adenoma It is important to have a report from a pathologist conversant with bronchial adenomata as the histology may otherwise be confused with that of an anaplastic carcinoma and the treatment consequently planned on a false diagnosis for example, a whole lung may be removed from a patient who should have been treated by a less drastic procedure such as lobectomy

The surgical treatment of a patient harbouring a bronchial adenoma must be selected from the following alternatives

1 Local treatment by bronchoscopy
2 Transthoracic removal of the tumour by bronchotomy
3 Resection of the lobe or lung bearing the tumour

Although there is no cure without surgery there are rare instances in which the surgeon may feel that the patient's interests are best served by not *interfering I have in mind two patients known to have adenomata, a man* aged 74 and a woman aged 67, who are both able to lead moderately active lives In neither case have I felt justified in operating as the surgical risks in my opinion exceed the dangers of the disease, particularly in the case of the woman, whose symptoms started 36 years ago

Local Treatment by Bronchoscopy

There are numerous cases on record in which removal of the tumour through the bronchoscope has been followed by apparent cure In some cases the tumour has simply been removed with biopsy forceps the procedure being repeated when necessary in others the tumour has been destroyed by repeated diathermy coagulation On other occasions eradication of the tumour has been attained by a combination of these methods, that is, by removing the main mass of the tumour with the biopsy forceps and cauterizing the area of origin with the diathermy current Diathermy coagulation is now condemned by most surgeons as it is very difficult if not impossible, to determine the depth to which necrosis has been produced Necrosis extending into the bronchial wall may be followed by sloughing of the tissues and subsequent infection or secondary haemorrhage Even if excessive necrosis is not followed by such dramatic events there is still the likelihood of a fibrous stricture occurring as a late sequel

Removal of the tumour has also been combined with local irradiation, either by placing a tube containing radium in the bronchus at the site of the tumour or by the insertion of radon seeds actually into the bronchial wall This form of treatment is no longer employed as it is now generally agreed that there is little, if any, evidence that bronchial adenomata are radio sensitive, so that attempts at local irradiation are not founded on a sound basis

Diathermy cauterization and local irradiation alike having been condemned, further consideration must be given to the indications for removal of the tumour through the bronchoscope with biopsy forceps This method of treatment is certainly attractive as the operation appears to be of such a minor nature, but it is essential to take into consideration the following facts

1 As previously mentioned, adenomata are frequently very vascular, so that attempts at piece meal removal may be accompanied by quite alarming blood loss
2 Reference has already been made to the high incidence of malignant change in these tumours, cancerous change may therefore supervene unless the entire tumour is removed
3 In most cases the bronchoscopist only sees the upper end of the intra-bronchial mass, so that it is impossible for him to say how far distally the tumour extends It may ramify distally, so far as to make total removal through the bronchoscope completely impracticable
4 The adenoma may be of the 'collar stud' type, an endobronchial growth being connected by a neck of tumour tissue passing between two bronchial cartilage rings with a mass outside the bronchus which may be much larger than the tumour within the bronchus (See Fig 151)
5 The great majority of patients with adenomata do not come to the thoracic surgeon until there are gross and irreparable secondary inflammatory changes (bronchiectasis or lung abscess) in the *bronchi* and lung tissue distal to the site of obstruction (See Fig 152) Bronchoscopic removal of the tumour would not therefore relieve the patient of all symptoms, although improvement might be expected as a result of relieving the bronchial obstruction

For these reasons bronchoscopic removal is to be recommended only in exceptional cases If the tumour appears to be not unduly vascular and to have a narrow bronchial attachment, and if careful radiological investigation including tomography fails to reveal any evidence suggesting an extension outside the bronchus, bronchoscopic removal may be attempted This applies particularly to cases in which there is no clinical or radiological evidence of irreparable septic changes distal to the tumour When such changes have

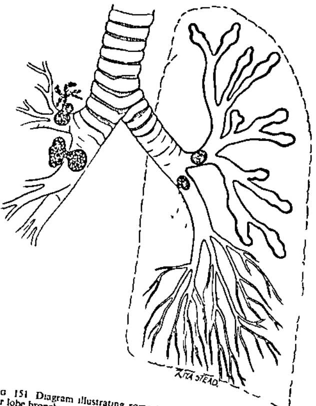


FIG 151 Diagram illustrating some types of adenoma In the left lower lobe bronchus a tumour is shown with a narrow ped cle and without secondary changes in the lobe distally this type is suitable for bronchoscopic removal In the left upper lobe bronchus an adenoma has obstructed the bronchus and caused secondary bronchiectas s In the intermediate bronchus on the right side a tumour of the collar stud type is depicted. In the right upper lobe bronchus the adenoma is drawn to show malignant infiltration starting from its upper pole



FIG 152 Photograph of a pneumonectomy specimen showing an adenoma in the left lower lobe bronchus projecting up into the main bronchus The lower lobe is completely destroyed by an abscess secondary to the obstruction of the bronchus by a tumour

occurred bronchoscopic removal may occasionally be justifiable in order to provide better bronchial drainage, either so as to improve the general condition of the patient prior to operative removal of the affected lung tissue, or as the final form of surgical treatment in subjects considered unfit for more radical procedures

In all cases in which bronchoscopic removal is undertaken as the definitive form of treatment regular follow-up examination by bronchoscopy is essential

Transthoracic Removal of the Tumour by Bronchotomy

From the foregoing comments on bronchoscopic removal of adenomata it must be obvious that there are very few cases in which thoracotomy will enable the surgeon to incise the bronchus, remove the whole tumour, and subsequently restore the continuity of the bronchus by suture, leaving an otherwise normal lung *in situ* Removal by bronchotomy in these cases free from irreparable inflammatory change distal to the tumour should, however, be born in mind as a possibility when performing a thoracotomy, particularly when the situation of the tumour would otherwise involve the sacrifice of the whole lung

Resection of the Lobe or Lung bearing the Tumour

In practice the attainment of symptomatic relief and freedom from recurrence of the tumour usually necessitates lobectomy or pneumonectomy The site of the tumour ascertained by bronchoscopy will determine whether removal of the whole lung is necessary or whether lobectomy will suffice In this connexion it is worth emphasizing that an adenoma often projects proximally well above its bronchial attachment so that a tumour arising from, say the upper part of the left lower lobe bronchus, may project into the lumen of the main stem bronchus on a level with the upper lobe bronchial orifice In such circumstances incision of the upper part of the lower lobe bronchus will allow the proximal endobronchial projection to be withdrawn from the main bronchus like a finger from a glove, leaving enough of the lobar bronchus for suture Unnecessary removal of a healthy upper lobe is thus avoided

Lobectomy or pneumonectomy is performed by the dissection technique described in the discussion on treatment of bronchial carcinoma in the case of innocent tumours there is, of course, no indication for removing all the accessible lymphatic glands from the mediastinum

PAPILLOMATA

Squamous-celled papillomata are very rare tumours which like the adenomata, usually occur in the large bronchi, but they differ from the adenomata in

showing no great vascularity and no tendency to extend outside the bronchus The frequency of malignant change is unknown although on general principles of pathology, such change is certainly a possibility Bronchoscopic removal may therefore be undertaken with better prospects of cure than is the case with adenomata Papillomata like other intrabronchial tumours may be the cause of chronic suppurative changes in the lung distal to the tumour and these changes may call for treatment by lobectomy or pneumonectomy on their own account

CHONDROMATA, OSTEOMATA FIBROMATA HAMARTOMATA

For the purpose of discussing operative treatment these rare innocent tumours may be grouped together and considered according to their site of origin and the secondary changes produced

1 Those occurring in the large bronchi and visible by bronchoscopy
   (a) Without inflammatory complications distal to the tumour
   (b) With such complications
2 Those occurring in the lung beyond bronchoscopic visibility

Cases occurring in the larger bronchi visible by bronchoscopy and without inflammatory complications may be treated by bronchoscopic removal, although repeated follow up examination by bronchoscopy should be carried out in order to exclude recurrence Where secondary septic complications have occurred the only reasonable treatment is resection of the affected portion of the lung together with the tumour (see Fig 153)

Those occurring in the periphery of the lung and therefore not visible by bronchoscopy, may be discovered in the absence of symptoms as a result of routine radiography in other cases slight pain in the chest or the expectoration of some blood stained sputum may have led to X ray examination of the chest In either case the clinician is faced with the problem of deciding what treatment should be recommended for a patient in whom a well defined opacity within the lung has been demonstrated the exact cause of the opacity being unknown It is probable that the opacity suggests some sort of tumour although it may be difficult to distinguish an opacity due to a tumour from that caused by a localized inflammatory mass such as a tuberculoma

The greatest difficulty arises in distinguishing an innocent tumour from a peripheral circumscribed carcinoma in fact it is frequently impossible without operation to distinguish between the two unless the patient is kept under observation until an increase in size of the opacity or the appearance of metastases indicate the malignant nature of the tumour Obviously such a wait and see policy can never be justified unless the patient s condition precludes the possibility of successful operative treatment for, if the tumour

happens to be malignant, the delay will reduce the likelihood of cure by operation and may even render a previously operable tumour inoperable

For these reasons a patient with an innocent tumour in the more peripheral part of the lung almost invariably requires exploratory thoracotomy If, on



FIG 153 Photograph of a lobectomy specimen showing a chondroma in the left lower lobe bronchus with gross secondary bronchiectasis and abscess formation

exploration, the surgeon is satisfied that the growth is innocent, the operation will be as conservative as possible, resecting only that portion of the lung containing the tumour It is, however, rarely possible to remove the tumour without at least one lobe, although occasionally resection of a single segment of the lung (Segmentectomy) will suffice (See Figs 1 to 3, Chap I)

HAEMANGIOMATA

These tumours present clinically as two quite distinct types

(a) Cavernous haemangiomata in which there are relatively large arterio-venous communications in the pulmonary circulation, so that some

venous blood reaches the left side of the heart without passing through the pulmonary capillary bed and there is therefore a greater or lesser degree of cyanosis

(b) Capillary haemangiomata or haemangio endotheliomata in which there is no appreciable short-circuit of the pulmonary circulation (and therefore no cyanosis) these are rare tumours

The treatment of the latter type is exactly the same as that of other peripherally placed innocent neoplasms (q v)

Cavernous haemangiomata cause not only cyanosis but frequently also compensatory polycythaemia clubbing of the fingers and finally heart failure The simulation of cyanotic congenital heart disease is therefore very close but these changes can be reversed by resection of the portion of lung bearing the arterio-venous communications Unfortunately these tumours tend to be multiple and not infrequently bilateral so that pre operative investigation should include angiocardiography to demonstrate clearly the extent and distribution of the lesions

If the fistulous communications are limited to one lobe lobectomy is usually indicated

The operation does not usually present any particular difficulty pulsation of the affected area is often demonstrable and there may be some increase in the calibre of the vessels at the hilum It is however important to have the patient well hydrated at the time of operation and to maintain a high fluid intake during the post operative period as vascular thrombosis particularly in the cerebral circulation may be a disastrous complication For the same reason although intravenous fluids during the operation are desirable it is preferable to avoid giving blood unless there is real need for it

From the relatively few cases treated by lobectomy which have been reported it would seem that the mortality of lobectomy for cavernous haemangioma is higher than that of lobectomy for many other conditions owing to the risk of post operative thrombosis

TERATOMATA AND DERMOID CYSTS

Intrapulmonary teratomata and dermoid cysts are extremely rare and in the absence of infection present in the same way as other peripherally placed innocent tumours and call for similar surgical treatment An infected dermoid cyst which communicates with a bronchus may be mistaken for a simple lung abscess in such cases the real nature of the lesion may not be recognized until the affected lobe has been removed under the supposition that the lesion was a chronic lung abscess Very rarely expectoration of hair or sebaceous material has permitted a correct pre operative diagnosis and has indicated the futility of expecting a cure of the condition by any means other than resection

MALIGNANT TUMOURS

In discussing the general principles of the surgical treatment of primary malignant tumours arising from the bronchi or within the lung, the rare sarcomata and the various histological types of the all too common carcinomata will be grouped together In spite of the advances in radiotherapy it must be conceded that surgical removal of a malignant growth is the only procedure which offers any reasonable chance of prolonged freedom from recurrence, amounting in some cases to cure It is therefore imperative that the diagnosis should be reached at the earliest possible moment and that surgical removal should be considered most carefully in every patient in whom this diagnosis is made

The first step in the care of a patient suspected of suffering from a malignant neoplasm is to try and establish the diagnosis as conclusively as possible When this has been done the chances of successful removal have to be carefully assessed If successful removal is considered a possibility, it is necessary to decide whether resection of the whole lung should be aimed at or whether a more limited operation (lobectomy) may be justified If the surgeon finds evidence indicating that total removal of the tumour is not feasible, he must consider whether the relief of symptoms calls for any operative treatment Such palliative operations are briefly discussed on p 243

Diagnosis

This has been discussed in Chapter II, but it is worth emphasizing the importance of obtaining histological confirmation of the diagnosis if exploratory thoracotomy or radiotherapy are contemplated Such information can be obtained in about 60 per cent of cases by means of bronchoscopy, and this method of examination should never be omitted in any case in which operative removal is a possibility

In some cases, for example, those in which the tumour originates in a segmental branch of one of the upper lobes, the growth may only be visible through the bronchoscope by using an indirect vision telescope, and in these circumstances it may be impossible to obtain a piece of the tumour for section, but the fact that the tumour has been seen makes the diagnosis much more certain In these cases in which the tumour is only visible by indirect vision it is well worth passing the biopsy forceps into the upper lobe orifice and removing blindly a piece of tissue for section, as it frequently happens that the tissue thus removed is found to include a portion of growth

As previously mentioned in Chapter I, in some cases where bronchoscopic biopsy is not feasible, malignant cells may be found in the sputum or in secretions aspirated through the bronchoscope, but the surgeon should be cautious in accepting such evidence unless the examination has been made

by an expert in this special technique I have known a patient with a peripheral circumscribed opacity shown in the X ray films to be subjected to removal of the whole lung because a pathologist of great ability but without experience in this special technique, reported that cells highly suggestive of a malignant neoplasm' had been found in the sputum actually the lesion was a localized solid tuberculous focus

Aspiration biopsy is unquestionably a most valuable method of obtaining histological confirmation of the diagnosis in the case of peripherally placed tumours but in patients in whom operative removal is a possibility it does not seem sound practice to pass a needle into the suspected growth through the chest wall and pleural cavity knowing that these tissues will not be removed at operation Although there are numerous reports claiming that the procedure is innocuous in operable cases I feel that aspiration biopsy should only be performed in those cases in which it has already been decided that resection is not practicable

In spite of every effort to obtain histological proof of the diagnosis it is not infrequently necessary to undertake operation on clinical and radiological evidence alone This applies particularly to peripherally situated tumours but in the case of upper lobe neoplasms the growth may be quite close to the lobar bronchus and yet be inaccessible to bronchoscopic biopsy In such cases the surgeon must decide before opening the chest what operation he plans to perform as in doubtful cases exploration frequently fails to provide any further evidence regarding the nature of the lesions Occasionally a peripheral neoplasm will show the typical umbilicated appearance of a malignant tumour so that the diagnosis is no longer in doubt but more frequently the mass is indistinguishable from a chronic inflammatory lesion such as a chronic lung abscess or a tuberculoma Examination of lungs removed for bronchial carcinoma repeatedly shows that the growth itself is responsible for a very small part of the main mass most of which is composed of chronic inflam matory tissues secondary to bronchial obstruction caused by the growth the futility of relying on exploration for diagnostic purposes then becomes obvious Diagnostic errors should be rare if proper care is taken in my own practice in 51 cases diagnosed as carcinoma and treated by resection two proved to be lesions other than carcinoma (one a chronic lung abscess and one a solid tuberculous focus)

Assessment of Operability

Exploration of the chest with a view to resection must only be undertaken if the patient s general condition offers a reasonable chance of his surviving resection and if there is no evidence that total extirpation of the growth is impracticable With regard to the patient s general condition allowance

must be made for the fact that the disease itself is lethal, so that great risks are justified Operation is therefore contra-indicated *only when there is* evidence that the chance of survival is minimal

Although age *per se* is not of particular significance, a successful result is most unlikely after the age of 70 Many patients between 60 and 65 withstand the operation without causing any anxiety, although gross disturbance of cardiac *rhythm in the post-operative* period is much more common in the older age-groups Severe wasting and cachexia indicates that the patient s reserve is limited and the chances of recovery from operation are therefore diminished *in any case such signs usually mean that the growth has extended* beyond the bounds of operability It is important to distinguish between wasting and natural thinness for, generally speaking, the lean patients convalesce from operation *more easily than those of heavy build* Degenerative changes in the arterial system are of more serious significance than valvular disease of the heart, provided the latter is fully compensated I have seen a patient with quite severe mitral stenosis (see Figs 154 and 155) and another with a mild degree of syphilitic aortic regurgitation recover from lobectomy and pneumonectomy respectively Hypertension is an unfavourable sign as it is usually associated with some degree of arterial degeneration, which increases the likelihood of circulatory failure appearing during the first *post-operative week however, in the absence of other unfavourable* factors, a raised blood pressure, unless extreme or associated with marked impairment of renal function, is no contra indication to operation Persistent hypotension is often of more grave portent than hypertension as it is usually indicative of a circulation which is already failing

Chronic bronchitis or emphysema or a combination of the two conditions in the 'good' lung mean that complications are likely in the post operative period and that in the event of recovery the patient's functional capacity *may be very limited On the other hand, it is often exceedingly* difficult to forecast the post operative events with accuracy, so that resection is frequently justified in the presence of quite severe contralateral bronchitis and emphysema

The difficulty of assessing correctly the importance of these disorders in the contralateral lung is illustrated by two cases, one a man of 60 who had been in hospital 5 years previously with dyspnoea due to emphysema and bronchitis, and the other a man of 51 who had suffered from asthma since childhood and *in later years from* bronchitis and emphysema, both of whom had a smooth convalescence after pneumonectomy for carcinoma, and both claim that they are now less breathless than before operation

As patients requiring operative treatment of bronchial carcinoma are often of an age at which prostatic enlargement is starting to give trouble, inquiries



FIG 154 (anterior)

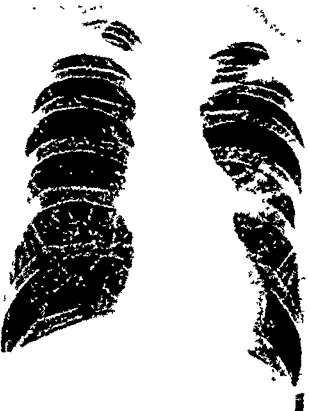


FIG 155 (lateral)

FIGS 154 and 155 Anterior and lateral radiograms of the chest of a man aged 43 with a circumscribed carcinoma in the apex of the left lower lobe The patient also suffered from mitral stenosis and the shadow of the enlarged left auricle can be seen in the anterior radiogram A left lower lobectomy was performed and *the patient is well and working 9 years after operation*

concerning micturition should be made and the patient examined for evidence of prostatic enlargement if there is any doubt on this point Prostatic enlargement would be no reason for delaying operation on a bronchial carcinoma but, if it is discovered before operation, post-operative retention of urine may be prevented or at least recognized and treated at its onset

The foregoing is an attempt to discuss those factors which are unrelated to the growth and which may influence the surgeon in reaching a decision whether to operate, but the chances of a patient being able to survive pulmonary resection can only be assessed with any degree of accuracy by someone with considerable experience It is perhaps worth mentioning here that under modern conditions the operation itself is not the stumbling block, for the patient's condition at the end of operation very rarely gives rise to any anxiety it is during the first week after operation that the troubles are most likely to arise The growth may extend beyond the limits of possible extirpation, either as a result of extrathoracic haematogenous or lymphogenous metastases or because of extension into irremovable tissues within the thorax

The more common sites of extrathoracic metastases are the brain, the lymph nodes in the neck and axillae, the liver and the bones Localizing signs of cerebral metastases are frequently absent persistent headache is commonly the only symptom or sign of such deposits, and in patients not ordinarily subject to headaches this symptom is almost pathognomonic of spread to the brain The lymph nodes in the neck and axillae are readily accessible to clinical examination and special care should be given to the palpation of those at the root of the neck, particularly when the growth has its origin in an upper lobe Abdominal palpation for evidence of hepatic enlargement cannot be too carefully performed in rare instances, when there is serious doubt regarding the presence of metastases in the liver, visual examination by peritoneoscopy may be of value With regard to osseous metastases which are most commonly found in the vertebrae, ribs, long bones, and skull it is the practice of some surgeons to undertake routine pre operative radiography of these bones, but this seems an unnecessary extravagance On the other hand, obstinate aching pain in the region of any of these bones certainly calls for the most careful X-ray examination, although the absence of radiographic changes does not necessarily exclude the presence of bony metastases

Evidence that the growth has extended within the thorax beyond the limits of operability may be found on clinical examination thus signs of superior vena caval obstruction or of involvement of the brachial plexus must be accepted as evidence of inoperability Likewise the presence of Horner's syndrome indicates destruction of the inferior part of the cervical sympathetic chain due to extension of the growth into an irremovable area Chest radiograms may reveal secondary deposits in the opposite lung or spread of the

growth into the mediastinum or into an irremovable part of the chest wall
With regard to chest-wall invasion, it is of course possible to resect a portion
of the chest wall together with the lung, but this is only practicable where
there is a reasonable margin between the area of involvement and the
vertebral column X-ray investigation should as a matter of routine include
fluoroscopy in order to observe diaphragmatic movement paralysis of the
diaphragm on the affected side almost invariably means that the growth
cannot be removed, but in rare instances the phrenic nerve may have been
destroyed as it passes over the pericardium, so that resection of the growth
together with the nerve and a portion of pericardium may still be possible
I have only known this to be the case in one patient

In some cases extension of the growth into the mediastinum may only be
demonstrable by radiological examination of the oesophagus after taking
barium emulsion by mouth the routine pre-operative investigation of all
cases of bronchial carcinoma should therefore include both fluoroscopic and
radiographic examination of the oesophagus Constant narrowing or irregu-
larity of the outline or deviation from the normal course are signs of inoper-
ability unless the deviation is in the region of the primary lesion and away
from the hilar region, in which case the mere size of the growth may be
responsible for deviation without invasion of the mediastinum

Clinical and radiological evidence of a pleural effusion is not necessarily
an indication of inoperability as the effusion may be of an inflammatory
nature due to infection of the lung distal to the neoplasm If there is a history
of an effusion which was transitory and which has been absorbed by the time
the patient reaches the surgeon, it is almost certain that the fluid was due to
infection and operation is therefore in no way contra indicated Where the
fluid persists a sample should be aspirated for examination if this is diffusely
blood-stained or contains malignant cells the case must be regarded as
inoperable If the fluid is purulent or obviously of an inflammatory nature
and there is no other evidence that the tumour is irremovable, exploratory
thoracotomy should be performed with a view to resection of the growth,
although the technical difficulties may be considerable and persistent infec-
tion of the pneumonectomy space may impair the result The latter complica-
tion has occurred in both of two patients on whom I have been able to perform
a pneumonectomy in the presence of an empyema If cytological or bacterio
logical examination of the fluid before operation leaves doubt as to the cause
of the effusion, it may be worth while replacing the fluid with air and examin-
ing the pleural surfaces with a thoracoscope if the pleura is then seen to be
infiltrated with growth the case is clearly inoperable

Bronchoscopy is also invaluable in assessing operability At this examina-
tion the movements of the vocal cords are carefully examined as it is not

uncommon for a carcinoma of the left lung to extend into the mediastinum and destroy the left recurrent laryngeal nerve The hoarseness of voice caused by paralysis of a vocal cord would naturally lead the clinician to suspect this complication prior to bronchoscopy, but examination of the cords is neces sary for confirmation Theoretically it might be possible to remove the lung together with carcinomatous tissue involving the nerve as it passes below the aortic arch, but this never proves to be the case in practice, so that a paralysed cord must be accepted as evidence of inoperability

Other indications that the growth has extended beyond the limits of operability include compression or erosion of the trachea by cancerous paratracheal glands, the presence of carcinomatous tissue proximal to the site at which the bronchus would be sectioned, widening of the carina due to involvement of the inferior tracheo bronchial glands, and narrowing or rigidity of a main bronchus consequent to neoplastic enlargement of the adjacent glands (see Fig 156) Slight widening of the carina should not exclude the patient from the possible benefits of operation, as this may occur when the inferior tracheo-bronchial glands are enlarged as a result of infection If there is no evidence that total removal of the growth is impossible and if the patient's general condition is considered to warrant an attempt at resection, the surgeon must then decide whether it is necessary to remove the whole lung or whether lobectomy would suffice and be preferable

Choice of Method of Resection

The aim of all cancer operations is to remove *en bloc* the whole primary growth and the regional lymphatic glands together with the intervening lymphatic vessels The only means of achieving this object in the case of bronchogenic neoplasms is to remove the entire lung together with any accessible mediastinal lymph glands pneumonectomy should therefore always be the operation of choice whatever the position of the primary growth It has been suggested that lobectomy is adequate treatment for the peripheral type of carcinoma, and this may be so in some cases (Fig 154), but it must be emphasized that the removal of regional lymph nodes is much less radical with this operation than with pneumonectomy This fact probably explains the relatively high incidence of lymphatic recurrence in some series of cases of peripheral carcinoma treated by lobectomy, although Neuhof (Neuhof and Aufses) does not accept this explanation

The importance of not relying on lobectomy unless there is some very real contra-indication to pneumonectomy was demonstrated by a woman aged 50 who was shown to have a circumscribed opacity about the size of a golf ball in the apex of the left lower lobe a diagnosis of carcinoma was made and the left lung together with the glands at the hilum were removed although

the primary growth appeared completely circumscribed, one of the lymphatic glands adjacent to the main bronchus and close to the tracheal bifurcation was found to be diffusely infiltrated by carcinoma If a lobectomy instead of a

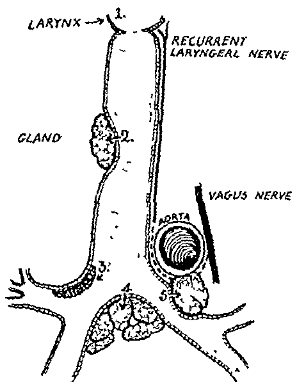


FIG 156 Diagram to illustrate extension of the growth such as to make total operative removal impossible a condition which may be recognized by bronchoscopy

pneumonectomy had been performed this gland would not have been removed so that evidence of local recurrence would presumably have appeared fairly soon after operation actually the patient continues in good health 2½ years after the pneumonectomy

Lobectomy for primary malignant growths should therefore be restricted to the treatment of patients who have a peripheral type of growth and whose cardio-respiratory reserve is such that pneumonectomy would not only be a dangerous operation but, if successful, might be expected to result in limitation of the patient's activities to such an extent as to preclude his following any but a sedentary occupation

It is obviously desirable to know what proportion of those patients who come to hospital with bronchial carcinoma can rightly be recommended to undergo exploration of the chest with a view to resection of the growth The published figures vary enormously, which is not surprising in view of the selection which is bound to occur for example, there will be a natural tendency to send patients whom the practitioner feels might be operable to institutions having a reputation for this form of surgery, whereas clearly inoperable cases might be sent elsewhere In addition some surgeons are prepared to take much greater risks than others so that an individual case may be deemed inoperable by one surgeon and operable by another Fortunately the possibilities of surgical treatment are now more widely appreciated by the profession so that the practitioner realizes the importance of making the diagnosis at the earliest possible moment, with the result that the percentage in which resection is feasible appears to be gradually rising This is well shown by Brock (1950) who found that out of 800 cases seen between 1941 and 1948 thoracotomy was performed in 172 and resection of the growth was undertaken in 106, i e an operability rate of 13 25 per cent However, the operability rate for each of the last 4 years was 15, 13, 21, and 23 per cent respectively, which shows a most encouraging upward trend

So far the discussion has been confined to primary broncho pulmonary neoplasms, but we must also consider whether surgery has any place in the treatment of a solitary pulmonary metastasis due to haematogenous spread from a primary lesion elsewhere This obviously depends on whether a pulmonary metastasis is ever truly 'solitary' Seiler and others (1950) were able to find in the literature 62 cases in which a pulmonary metastasis had been excised and, although the great majority of these patients died within a short time of the operation, there were 9 who were stated to be alive 3 or more years after removing the metastasis, and it is possible that a few of the many others who were recorded soon after operation may have survived for this length of time The longest period of survival which followed sub-total lobectomy for the removal of a secondary deposit from a growth of the fibula was 18 years (Edwards, 1946) Another striking case was that of Barney [illegible] for their patient was subsequently reported by Barney

tomy These cases must allow the conclusion that pulmonary metastases are sometimes genuinely solitary

The clinician is therefore justified in considering excision if the primary lesion has been apparently eradicated and was of relatively low grade malignancy, and if there is no evidence of growth elsewhere in the body (Churchill 1940) From the data available the pulmonary met s most likely to be an isolated lesion if the primary disease was a c o the large bowel kidney or ovary or a slow growing sarcoma (Sc 1950) If it is possible to remove the metastasis by lobectomy th s p ould be performed as there is no indication for the extensive re n hatic nodes which accompanies pneumonectomy

Preparation for Operation

If thorough investigation has led to the opinion that removal of the growth either by pneumonectomy or lobectomy is a practical proposition preparation of the patient for exploratory thoracotomy should be started at once First it is desirable to explain to the patient that an operation is necessary owing to the presence of a progressive disease of the lung which can only be cured by surgery It is preferable to avoid telling the patient the exact nature of the disease and the type of operation contemplated as this information is liable to cause alarm which may have harmful effects both before and after operation In spite of the gravity of the disease itself the patient should not be coerced into accepting operation against his wishes as such patients will not co operate during the post operative period and consequently almost invariably succumb

In all cases a physiotherapist properly trained in breathing exercises should teach the patient to improve thoracic movement on the good side and to increase diaphragmatic function The physiotherapist should take this opportunity of explaining what will be required of the patient immediately following the operation emphasizing especially the importance of expectoration however painful it may be In those cases in which the growth is complicated by secondary infection treatment with penicillin or other suitable chemotherapy is often useful in improving the patient s condition and reducing the quantity of sputum Likewise postural drainage may lead to improvement but it is of little value if there is gross bronchial obstruction by the growth In these circumstances the surgeon is occasionally justified in attempting to restore free drainage by bronchoscopic removal of endobronchial portions of the tumour although it is usually preferable to proceed with exploratory thoracotomy rather than waste valuable time with such manœuvres unless the patient s condition is very poor Finally it is advisable to acquaint the patient with the method of oxygen administration which may

be employed after returning from the theatre so that he may not look upon this as a sign of impending death

In the past an attempt to induce an artificial pneumothorax was often made about 1 week before operation especially in 'bad risk cases, as this was considered to reduce the disturbance caused by removal of one lung, this seems to be sound theoretically, but there is little evidence that the patients thus treated gained any advantage, and most surgeons have therefore abandoned the practice

Anaesthesia (Contributed by Dr R Machray)

The choice of method of anaesthesia used for pneumonectomy is guided by two special considerations the correction of disturbances arising from an open pneumothorax and the control of secretions from the diseased lung An open pneumothorax causes a variable amount of limitation of respiratory capacity So far as adhesions permit it the lung on that side collapses and the mediastinum is drawn over to the closed side During inspiration this mediastinal displacement is greatly increased but during expiration a partial return takes place this movement is termed 'mediastinal flap' The sound lung is therefore not only permanently decreased in size but expansion on that side is diminished according to the extent of mediastinal movement The reason for these changes is that gas displacement through the thoracotomy opening is easier than displacement through the air passages The mode of correction therefore lies in applying pressure during the inspiratory phase sufficient to overcome this disadvantage Correctly done this can reduce mediastinal flap to a minimum and so make respiratory exchange entirely adequate and give more satisfactory operating conditions This is assisted respiration' If for any reason the improvement is disappointing then spontaneous movement should be suspended and ventilation continued entirely by the anaesthetist This is 'controlled respiration'

Since it is only with an unconscious patient that such control can be exercised, general anaesthesia is almost always employed The most commonly used technique at the present time is administration of pentothal and curare in divided doses the patient breathing or being ventilated with a half and half mixture of nitrous oxide and oxygen using a closed circuit machine Such a method in addition to its anaesthetic advantages permits the free use of the diathermy An endotracheal tube is always passed and the movements of controlled respiration carried out either by manual pressure on the rebreathing bag or with a machine or pulsator Apnoea is produced under these conditions by a combination of respiratory depression moderate hyperventilation, and peripheral muscle paralysis

Control of secretions can be accomplished in two ways They can be

confined to the diseased lung by the placing of a bronchial block
main branches of the affected side. If th
difficult to
the up
such c
the left side. Alternatively ... to use an endo-bronchial anaesthetic ... obstructing the trachea. In
using the prone position with the head ... secretions can be kept from the health
secretions
should
over th
much less
and, when
... or any doubt exists, ... supplementing with suction, should be employed at the end of the operation.

After induction of anaesthesia an intravenous
and maintained thr
the infusion but
that at which bl
during a pneumonectomy varies from 1 to 2 pints to as much as 5 or 6 pints. ... being lost through the operation ... rate estimated to equal
Transfusion of quantities much exceeding that lost surgically may cause pulmonary oedema and should therefore be avoided. On the other hand the rate of transfusion must be increased before the signs of excessive blood loss (a rising pulse rate and a falling blood pressure) appear.

Operative Technique

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The chest is explored through a postero-lateral incision (see Fig. 157) which should sweep well below the inferior angle of the scapula so that the latissimus dorsi and serratus anterior muscles may be divided close to their origins. The anterior end of the incision should extend somewhat beyond the anterior axillary line as a long incision through the thoracic wall can be spread with less force than a short one. The chest may be opened by removing a rib from the tip of the transverse process to the costo-chondral junction and then incising the underlying periosteum and parietal pleura: the 5th rib is selected if a pneumonectomy or upper lobectomy is being contemplated, and the 6th rib for a lower lobectomy: the corresponding intercostal bundle is divided

posteriorly between ligatures One inch of the posterior end of the rib above or below may be removed in addition if wider [illegible]



FIG 157 Photograph of scar of postero lateral thoracotomy incision used for a left pneumonectomy

the corresponding intercostal bundles Adequate exposure is then obtained by the use of some form of rib spreader The practicability of resection must now be finally determined Neoplastic nodules scattered on the parietal pleura metastases in irremovable mediastinal glands, extension of the primary lesion into the cellular tissue of the mediastinum or invasion of an irremovable part of the chest wall signify unequivocally that the growth cannot be resected with any hope of a successful result

Bronchial neoplasms are especially liable to extend medially around the pulmonary vein which drains the blood from the affected lobe this area

should therefore be examined with particular care before commencing the resection If the growth has spread as far as the pericardium the latter should be opened anterior to the area of invasion and the intrapericardial portions of the veins and the auricular wall examined for the operation should only be abandoned when there is no hope of sectioning the veins or even the auricle medial to the growth It is more difficult to perform this preliminary intra pericardial exploration which is occasionally necessary when the patient is in the prone position In a patient in whom pre operative investigation has led to the conclusion that lobectomy would be preferable to pneumonectomy careful examination must be made to see that there is a reasonable chance of total extirpation of the growth by removing only the affected lobe intra thoracic exploration may show that this is quite impossible for example a peripheral growth may have transgressed an interlobar fissure making pneumonectomy the only practicable operation The technique of pneumo nectomy and lobectomy will now be considered separately

Pneumonectomy

After confirming operability the first aim should always be to place a clamp across the bronchus close to the trachea so that the surgeon no longer depends on the anaesthetist to take care of secretions which may be expressed from the diseased lung When the lung is adherent to the chest wall only those adhesions which interfere with adequate exploration of the chest or with access to the bronchus should be dealt with before clamping the bronchus dense adhesions should be overcome by stripping the parietal pleura from the chest wall but intrapleural section is adequate for those of light texture In order to isolate the bronchus the mediastinal pleura is incised above and behind the hilum Branches of the vagus which pass to the posterior pul monary plexus and which are often accompanied by small blood vessels are divided after taking adequate haemostatic measures The dissection towards the origin of the bronchus should be made proximal to any visible lymphatic glands taking care to avoid the recurrent laryngeal nerve on the left side This dissection is carried upwards to expose the adjacent part of the trachea including the carina and the medial wall of the contralateral bronchus When the bronchus has been completely isolated a bronchial clamp is placed obliquely across it so that after section and suture of the bronchus there will be no pocket like projection from the tracheal lumen at the site of the divided bronchus This is easy on the right side but can only be accomplished on the left by applying considerable downward traction High division of the bronchus is probably the most important factor in the prevention of the sub sequent formation of a bronchial fistula

Each surgeon has his own method of dealing with the bronchial stump

Personally I prefer to divide the bronchus proximal to the clamp and to close the lumen with simple interrupted stainless steel sutures threaded on eyeless needles The bronchus is not divided at one stroke but piece by piece and the sutures are inserted and tied as the section progresses so that there is never a large air leak from the trachea This method ensures that there is *no contusion of the tissues at the line of suture* If the patient is in the face down position division of the bronchus at this stage is almost essential in order to obtain access to the pulmonary artery and superior vein

After dealing with the bronchus the pulmonary artery is isolated, doubly ligated with strong ligature material close to the pericardium, and divided after placing a clamp or another ligature on the distal end On the right side the proximal portion of the pulmonary artery cannot be isolated properly *without dividing a strong fascial layer which attaches the anterior surface of* the vessel to the adjacent part of the superior vena cava It has been suggested that on the left side the ligatures should be placed proximal to the ligamentum arteriosum, which then acts as a safety device preventing the ligatures slipping but this is unnecessary unless the proximity of the growth necessitates section of the artery very close to the heart The two pulmonary veins are treated in the same way as the artery As a result of the short extra pericardial course of *these vessels the tendency for the ligatures to slip is greater* than in the case of the artery, and consequently some surgeons prefer to place a transfixion ligature between two ordinary encircling ligatures As the dissection is carried down from the hilum the inferior tracheo bronchial glands below the carina are separated from the medial wall of the opposite main bronchus, from the pericardium in front, and from *the oesophagus behind so that they will be* removed together with the lung Finally any adhesions still present are separated and the pulmonary ligament divided so that the lung may now be removed The lymphatic glands, placed adjacent to the oesophagus and between the layers of the pulmonary ligament at its mediastinal attachment, should be left attached to the lung and removed with it (see Fig 158) The appearance of the mediastinum after removing the right lung in this way is *shown in Fig 159*

In those cases in which the growth extends too close to the pericardium to make division of the pulmonary veins external to the pericardium possible or reasonably safe, the sac should be opened and the vessels ligated *immediately* adjacent to the left auricle Similarly where necessary the artery may be divided at a more proximal *level by opening the pericardial sac* (Allison 1946) In a few cases in which the growth has extended so far medially that even intrapericardial ligature of the veins is impossible the lung may yet be removed by placing a non crushing clamp (such as the Crafoord aortic clamp) across the adjacent part of the auricle and making the section through

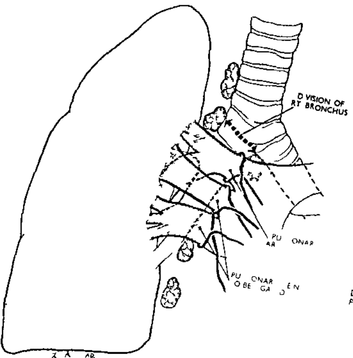


FIG 158 Diagram to show the site of ligation of the main vessels and the line of division of the main bronchus when performing a right pneumonectomy The lymphatic glands which should be removed together with the lung are indicated in the diagram

FIG 159 Drawing of the field of operation showing the appearance of the mediastinum after removal of the right lung

the auricular wall, which is subsequently sutured Intra-pericardial division of the main vessels is quicker and easier than the extra-pericardial operation but this does not justify opening the pericardial sac on the slightest pretext as there is a strong impression that post-operative cardiac irregularities (fibrilla tion, &c) are more common when the sac has been opened Before closing the chest an intercostal drain connected to a water-seal bottle is placed near the bottom of the pleural cavity

Lobectomy

In the operation of lobectomy the bronchus, the pulmonary artery, and the pulmonary vein leading to or from the lobe are treated in a way exactly analogous to that described for the hilar structures when doing a pneumonectomy The bronchus is clamped as early as possible and the level of section selected so that there is no blind pocket projecting at the site of suture The vessels are dissected out and ligated and divided separately If the neoplasm is in the right lower lobe the operation should include removal of the middle lobe, as the bronchus can then be divided at a much higher level so that there is a wider margin between the growth and the site of section

The technique of lobectomy will not be discussed further as this would involve a description of the anatomy of the hilum of each lobe and of the variations which may be found for these the reader is referred to other pub lished works (Blades and Kent, 1940, Churchill, 1940, Kent and Blades, 1942, Boyden, 1945)

Pleural drainage after lobectomy is provided for by a basal intercostal drain similar to that employed after pneumonectomy some surgeons insert in addition an intercostal catheter through the second or third intercostal space posteriorly and use this for mechanical suction under certain circumstances (see Post-operative Care)

'Tourniquet lobectomy' is the label applied to an operation in which all the hilar structures are temporarily included together in one single encircling ligature so that the lobe may be cut off and the hilar structures sutured *en masse* With this operation the site of section would be far too close to the growth and there is therefore no place for it in the surgery of bronchial carcinoma It is, however, amusing to reflect that the patient who has survived for the longest period (9 years) after resection of a growth by the author was done for the

as soon as the chest was opened

Post-operative Care

It is a wise precaution to give oxygen through twin nasal catheters or on a

B L B mask as a routine from the time of operation This may be unnecessary in robust subjects, but in the frail and elderly oxygen therapy should be continued for at least 24 hours, or for as long as there is the slightest cyanosis or dyspnoea at rest

It is convenient to maintain the intravenous infusion with glucose saline at a very slow rate during the first 24 hours so that excessive fluid loss by sweating or vomiting can be balanced at once by increasing the rate and further blood can be given if there is much lost through the pleural drain On the other hand the risk of overloading the circulation in these subjects is very real and should be avoided

Breathing and leg exercises and postural instruction are started under the guidance of a specially trained physiotherapist on the day after operation and are continued throughout convalescence

Purulent bronchitis, which may develop into broncho pneumonia is the commonest cause of morbidity and mortality after pneumonectomy It is in fact so common that one almost expects a patient to have a gradually increasing expectoration which becomes frankly purulent about the fourth post operative day Systemic penicillin, which is given as a routine for a least one week after operation, may help in controlling the infection but expectoration of sputum is probably more important in preventing and curing post operative bronchitis To facilitate expectoration sedatives should be given so that coughing is not too painful but the dose should not be sufficient to abolish the cough reflex Pethidine is very useful for this purpose although it is usually necessary to give some opiate as well Steam inhalations and saline expectorants such as ammonium chloride are valuable if the sputum is viscid and ephedrine may give relief when there is associated broncho spasm

Patients are nursed in the semi sitting position as this is found to be most comfortable but they should be encouraged to move about in bed so that sputum does not stagnate in the most dependent portions of the bronchial tree In cases of pneumonectomy the patient should also lie flat on the operative side for a short period (a quarter of an hour to one hour) night and morning so that gravity may help to drain sputum from the remaining lung Occasionally the patient fails to clear the air passages in spite of these measures to prevent retention of sputum in this case bronchoscopic aspiration in bed is necessary and may have to be repeated but the patient must be made to realize that he ultimately depends on his own efforts Retention of sputum in cases of lobectomy is discussed later under Management of the Pleural Space'

Irregularities of cardiac rhythm such as paroxysmal tachycardia auricular flutter, and particularly auricular fibrillation are of frequent occurrence, starting most commonly between the third and seventh days Flutter and

fibrillation are usually treated by some method of rapid digitilization so as to bring the ventricular rate down to a reasonable level With this treatment flutter is likely to switch to fibrillation, although an early return to sinus rhythm may occur As soon as the ventricular rate has been adequately slowed the dose of digitalis is reduced to that required to keep the rate within normal limits In my experience a return to regular rhythm has invariably taken place either during the period of digitalis therapy or shortly after discontinuing a course of one to two weeks' treatment Quinidine also may be used to treat flutter and fibrillation and it is possible that this drug may prevent these irregularities if given in the pre- and post operative periods

Management of the Pleural Space

1 *After Pneumonectomy* The intercostal drainage tube is connected to a water-seal bottle in the theatre if the connecting tube is occluded with a screw-clip which is released at intervals, say every 3 hours, blood and fluid escape from the pleural space and the mediastinum is unlikely to become grossly displaced, which so often occurs when the tube is continually open as the latter results in air being expelled from the chest every time the patient coughs or strains The intercostal tube is removed after 48 hours unless there is some special reason for continuing drainage At this time, as it is difficult or impossible to determine accurately the position of the mediastinum from clinical signs, a chest radiogram is taken in the ward it is usual to find the mediastinum displaced to some degree towards the side of operation, and this ma [illegible]
of [illegible]

As convalescence proceeds the air in the pleural cavity is gradually absorbed and is replaced with blood stained serous fluid In a few cases this fluid may form in excess and displace the mediastinum towards the opposite side, in this event some of the fluid should be removed by aspiration, repeating this if necessary, so that the mediastinum is maintained in a central position This method of controlling the amount of fluid in the space, and hence the position of the mediastinum, can be used during the first 48 hours after operation instead of inserting an intercostal drain in the theatre, but it involves more disturbance of the patient in the ward, and increases the work of the assistants

Ultimately the hemithorax becomes much reduced in size as a result of a rise in the position of the diaphragm, displacement of the mediastinum towards the side of the pneumonectomy, and contraction of the chest wall the small residual space is occupied by a 'sponge' of fibrin and fibrous tissue with serous fluid in its interstices (See Figs 160 to 162)

The final degree of mediastinal displacement varies from case to case It is generally, although not universally, agreed that gross displacement with

consequent distension of the remaining lung leads to reduced functional capacity and is therefore undesirable For this reason a few surgeons perform a thoracoplasty when the patient is fully convalescent from the pneumonectomy but this is a great ordeal for most of the patients Others have tried

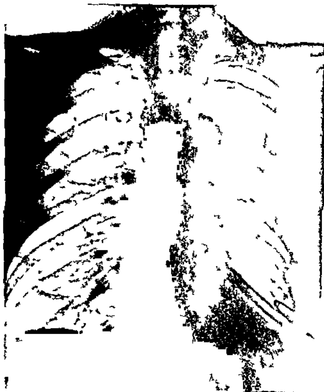


FIG 160 X ray appearances 1 day after left pneumonectomy for carcinoma The drainage tube shown is too long although satisfactory drainage has occurred due to the semi recumbent position of the patient

filling the dead space with various types of inert material at the time of operation but this procedure is still in the experimental stage (Grindlay and Clagett, 1949)

The displacement of the mediastinum is usually less marked in those cases in which the diaphragm rises high in the chest thus reducing the size of the hemithorax In order to obtain a satisfactory elevation of the diaphragm the muscle should be paralysed by excising a portion of the phrenic nerve and this is generally done at the time of pneumonectomy but in patients with a



Fig 161 Same case 7 weeks after operation

Fig 162 Same case 14 weeks after operation

that tube drainage will have to be maintained permanently unless some plastic operation is performed at a later date (See Fig 163)

2 *After Lobectomy* The essentials in the management of the pleural space



FIG 163 X ray appearances following a right pneumonectomy a month after which a bronchial fistula developed necessitating pleural drainage Iodized oil has been injected through the drainage tube and demonstrates persistence of the fistula

The operation was performed 7 years ago on a man of 39 for squamous-celled carcinoma he has worked without interruption as a skilled carpenter since leaving hospital and remains free from recurrence

following lobectomy are (1) Water seal tube drainage for 48 hours and subsequent aspiration of any bloody fluid which may persist or recur, and (2) the treatment of any complicating pleural infection or bronchial fistula on the same principles as those described for these complications in pneumonectomy The fundamental aim after lobectomy, however, is to have no pleural space to manage, that is to say the remaining lobe is encouraged in every

possible way to expand and remain expanded so as to fill the hemithorax This depends almost entirely on keeping the bronchi free of secretion by expectoration and the importance of getting the patient to cough up any sputum cannot be overstressed Expectoration may be aided by posture e g



lying the patient on the good side for periods of half an hour to one hour twice a day If the remaining lobe does collapse efforts to restore the air way by coughing and posture should be redoubled If in spite of this the lobe remains collapsed after 12 hours the patient should be bronchoscoped in bed and the bronchi cleared of secretion by suction (See Figs 164 to 166) It is the practice of some surgeons to introduce an intercostal catheter at the apex of the pleural cavity posteriorly (in addition to the basal drain) at the time of operation through this tube (the apical sucker) mechanical suction is

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2 *After Lobectomy* The essentials in the management of the pleural space



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FIG 164 Chest radiogram demonstrating the development of collapse of the upper lobe following left lower lobectomy and lingulectomy The film was taken the day after operation and shows an air-conta ning upper lobe almost filling the hemithorax

lying the patient on the good side for periods of half an hour to one hour twice a day If the remaining lobe does collapse efforts to restore the air way by coughing and posture should be redoubled If, in spite of this the lobe remains collapsed after 12 hours, the patient should be bronchoscoped in bed and the bronchi cleared of secretion by suction (See Figs 164 to 166) It is the practice of some surgeons to introduce an intercostal catheter at the apex of the pleural cavity posteriorly (in addition to the basal drain) at the time of operation through this tube (the 'apical sucker') mechanical suction is

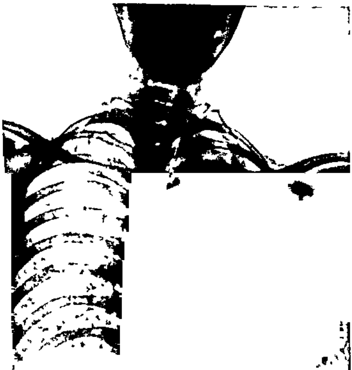


FIG 165 Same case 2 days after operation showing total collapse of upper lobe

FIG 166 Same case film taken later the same day showing re-aeration of upper lobe after bronchoscopic aeration

applied if the remaining lobe shows any signs of collapse or has failed to reach the apex of the pleural cavity on the morning after operation

Results of Operation

Of those patients submitted to exploratory thoracotomy the proportion in which resection of the growth is found to be practicable is about 60 per cent (Brock 1950 62 per cent , Sellors *et al* 1947 53 per cent Oschner *et al* 1948 , 63 per cent Gagnon 1948 56 per cent) Churchill (1948) added the figures of nine authors together and found that out of 782 cases in which the chest was explored 432 (55 per cent) were treated by resection

In the practice of most thoracic surgeons the proportion of patients submitted to exploratory thoracotomy without success in removing the growth is slowly decreasing This decrease is partly due to the fact that technical manœuvres such as intra pericardial dissection have been developed so that resection may become practicable in some cases which previously would have been abandoned as inoperable In addition as a result of increased surgical experience, better judgement is undoubtedly used in the selection of cases suitable for exploration

Published figures for operative mortality differ considerably This may be due in part to the fact that the term operative mortality has no strict definition but the varying experience and ability of the surgeons and their teams must also have their effect on the figures There is little doubt however that the most potent influence on operative mortality is the willingness or otherwise of individual surgeons to accept bad risk patients for surgical treatment consequently a low death rate after operation may not be a measure of the excellence of the surgical treatment but rather be an indication that surgery is not being offered to some who might benefit from it The published figures of competent surgeons show that between 10 and 25 per cent of patients treated by pneumonectomy die before leaving hospital and that there is a definite tendency towards lower figures during the last few years

The functional capacity of those treated by resection is obviously a matter of great concern especially as there are still some who believe that a successful pneumonectomy means sentencing someone to a life of miserable invalidism In this regard lobectomy needs little consideration as patients treated by this operation suffer little if any diminution in their capacity fo physical exertion provided breathing exercises are intensively employed during convalescence so that the remaining lung tissue compensates for the part removed Exercise tolerance after pneumonectomy varies considerably according to the age of the patient the condition of the remaining lung and the cardiovascular system and perhaps the degree of mediastinal shift A patient under 55

without evidence of disease in the remaining lung or in the cardiovascular system is unlikely to suffer much limitation in his activities, unless these involve strenuous physical effort For example, a locomotive fireman aged 41, who [illegible]
drive anc [illegible]
On the ot[illegible] [illegible]atients over 60 and especially those over 65 *must expect* to be handicapped to some degree by dyspnoea on exertion this is likely to be more severe when the healthy lung has been affected by emphysema or chronic bronchitis Even so it is most exceptional to find a pneumonectomized subject unable to perform the duties of a 'white collar' worker Sometimes exercise tolerance may be very low for several months, but the patient must not be allowed to become discouraged as it is surprising how some of these cases gradually improve as a result of persistence with breathing exercises and graduated physical effort

The value of surgery in the treatment of bronchial cancer depends largely on the prognosis of those patients in whom the growth has been successfully removed It is only 17 years since Evarts Graham (1933) performed the first successful pneumonectomy for a malignant tumour, and operative treatment was not frequently rewarded by success until the last decade, so that figures recording late results are still very limited It is, however, already clear that recurrence is depressingly common, but this could hardly be otherwise, for bronchial growths are well known for their capacity to produce haematogenous metastases Lymphatic deposits are also common but these may all be included in the tissues removed if the operation is a radical pneumonectomy Consequently, death due to recurrence is more often due to extrathoracic blood born metastases than to intrathoracic recurrence When studying statistics relating to the time of survival after operation it must be remembered that the average duration of life from the onset of symptoms of bronchial carcinoma is 9 months

In 1947 Graham, in discussing a paper by Adams (1948) on carcinoma of the lung, stated that of 53 patients who were treated by pneumonectomy prior to 1942, i e more than 5 years previously, 15 (28 per cent) were alive and well Ochsner and others (1948) reported that of 40 patients treated by pneumonectomy 5 or more years previously 11 (27 5 per cent) had survived 5 years but it is disappointing to note how badly the next 40 cases must have fared for, out of 80 patients treated 3 or more years previously only 16 (20 per cent) survived 3 years

Although these figures are not too encouraging, it is clear that surgery offers some patients suffering from bronchial carcinoma a chance of at least carrying on a useful life for a number of years The period of freedom from recurrence has been sufficiently long in some cases to justify the term 'cure'

However, the value of surgery in the treatment of cancer does not lie solely in its ability to produce a few people with lasting freedom from recurrence, for there are many others for whom life is prolonged and made active and enjoyable, and these patients should not be considered complete therapeutic failures There is therefore no excuse for failing to attempt an early diagnosis on the grounds that surgical treatment has little to offer

PALLIATIVE OPERATIONS

Surgery is sometimes employed to relieve distressing symptoms in patients suffering from manifestly incurable malignant disease of the chest The symptoms which may call for such relief are (1) Intractable pain due to malignant invasion of the chest wall or brachial plexus, and (2) Severe toxaemia caused by suppurative complications such as empyema and lung abscess, the latter may also be responsible for frequent and exhausting paroxysms of coughing

The pain due to chest wall erosion is very variable but it can be extremely severe and beyond relief by anodyne drugs Radiotherapy is on the whole disappointing in its ability to ease pain of this type (see Chap XIII), so that interruption of the nerve pathways responsible for carrying the pain impulses may be the only means of alleviating the patient's misery An attempt to relieve the pain by radiotherapy is usually worth while before resorting to surgical measures unless the pain is exceptionally severe or the area of irradiation would include the operative site of nerve section, as for example in the case of a paravertebral tumour for which posterior rhizotomy had been planned if radiotherapy failed in its object

If the chest wall erosion is placed lateral to the paravertebral sulcus, the intercostal nerves supplying the affected area may be blocked medially with procaine, and if this gives temporary relief more prolonged alleviation may sometimes be obtained by the injection of an oily solution of procaine (proctocaine) If the effect of these measures is satisfactory but too transient, the intercostal nerves may be divided through a vertical incision along the lateral border of the erector spinae (sacrospinalis) muscle

Unfortunately the chest wall erosion frequently extends medially into the paravertebral sulcus making it impossible to interrupt the sensory pathways lateral to the vertebral canal In such circumstances the nerve fibres which carry the pain impulses may be interrupted either by division of the appropriate posterior nerve roots (posterior rhizotomy) or by sectioning the spino-thalamic tract of the opposite side at a level well above the site of the pain (antero-lateral chordotomy) Posterior rhizotomy is infrequently performed as the pain is unlikely to be relieved unless the root section includes at least one root above and one root below the area of distribution of the pain,

consequently it is usually impossible to divide sufficient roots without endangering the blood-supply of the spinal cord Another disadvantage of rhizotomy is the fact that for some unknown reason the pain tends to recur even when there is complete insensibility of the area in which the pain is felt, a disadvantage which also applies to intercostal neurectomy Further it must be remembered that the loss of sensation which follows posterior rhizotomy includes the sense of posture and of touch which is a serious drawback when the first dorsal and lower cervical roots are involved as occurs with the 'superior sulcus tumours' described by Pancoast

Chordotomy is, therefore, generally the preferred method of relieving pain by nerve section, but it may be well to emphasize the importance of dividing the spino-thalamic tract some five or six segments above the uppermost limit of the area of pain distribution For example, the tract must be divided at the level of the second or third cervical segment in order to relieve pain caused by malignant invasion of the lower part of the brachial plexus, although division of the pain fibres as they cross the mid line at a lower level has been used successfully by some surgeons

It is sometimes stated that pain should always be relieved by drugs and that there is never a need to have recourse to surgery There is no doubt that operative treatment should be restricted to a very limited group, but these selected few include some of the most grateful patients ever to be met

The subject of relieving surgically the misery caused by pain would not be complete without mention of leucotomy which has been used to abolish the anguish caused by pain without actually removing pain perception, but this method of providing relief is not generally acceptable because of the character changes which are likely to follow leucotomy

Operative treatment of septic complications of inoperable growths in order to improve the patient's sense of well-being are rarely, if ever, necessary or effective The toxic effects of empyemata can nearly always be reduced to a minimum by repeated aspiration and the intrapleural injection of suitable antibiotics, which treatment is much preferable to condemning the patient to tube drainage for the rest of his short life Alleviation of the symptoms caused by pulmonary suppuration is a more difficult problem, although systemic penicillin therapy, combined with postural drainage if the pus can escape through the bronchial tree, may be a great help Rib resection under local anaesthesia and the provision of external drainage may be justified if chemotherapy fails and the patient is being exhausted by the expectoration of large quantities of pus, but the disadvantages of a draining wound with the possibility of secondary haemorrhages are likely to be more burdensome to a dying patient than the symptoms for the relief of which the operation was performed

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THE SURGICAL TREATMENT OF NEW GROWTHS OF THE MEDIASTINUM

The difficulty in deciding correctly the pathological nature of a mediastinal tumour in the living subject has been mentioned in previous chapters but a correct pathological diagnosis is of importance to the surgeon as the indications for surgical treatment depend to some extent on the nature of the tumour In order to limit the discussion on the indications for operation the circumstances which should lead a surgeon to advise against operation will first be reviewed briefly

The first essential is to exclude irremovable non neoplastic lesions such as aortic aneurysms in doubtful cases angio cardiography may be helpful and if there is still doubt after this examination it may be justifiable to define the shadow cast by the aorta by filling it with radio opaque fluid introduced through a fine catheter passed up the radial artery

Operation should also be avoided in the case of tumours of lymphomatous nature such as lympho sarcoma and lymphadenoma Many of these cases may be recognized by careful clinical and haematological studies but if these investigations do not help in the diagnosis and the tumour is still suspected of being lymphatic in origin a short course of X ray therapy may be given (see Chap XIII) for lymphatic tumours are extremely radiosensitive and may be recognized by the rapid reduction in size which accompanies and follows X ray treatment (see Figs 167 and 168)

Carcinomatous metastases frequently occur in the mediastinum usually originating from a primary bronchial lesion but occasionally secondary to an

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Carcinomatous metastases frequently occur in the mediastinum usually originating from a primary bronchial lesion but occasionally secondary to an



Fig 167

Fig 168

Figs 167 and 168 Radiograms of the chest of a boy aged 16 Fig 167 shows a massive mediastinal tumour Fig 168 was taken after X ray therapy There is an interval of 9 months between these two films but actually a marked diminution in the size of the tumour could be appreciated within 3 weeks of starting treatment Death occurred 2 years later from abdominal metastases which were shown to be lympho sarcomatous

extrathoracic growth as the primary lesion may be relatively insignificant it is sometimes overlooked and consequently the mediastinal mass receives the false diagnosis of a primary neoplasm of the mediastinum for which surgical removal may be recommended Such an operation would of course be futile and harmful but it should never occur if the clinician is constantly alert to recognize these cases

Finally it must be obvious that it is impossible successfully to remove a primary mediastinal tumour in which malignant degeneration has led to invasion of essential structures Obstruction to the venous return in an innominate vein or in the superior vena cava suggests such malignant invasion but venous obstruction may occur with entirely innocent tumours especially those of thyroid origin Paralysis of a phrenic or recurrent laryngeal nerve almost certainly indicates malignant infiltration of the mediastinum although such palsies have been known to follow simple stretching by a large innocent tumour It is quite certain however that endoscopic or radiological evidence of invasion of the main air passages or of the oesophagus are absolute contra indications to an attempt at operative removal

It may now be profitable to consider the indications for operation assuming that the correct pathological nature of the tumour is at least suspected and that the contra indications to surgery described above are not present Apart from rareties the tumour is likely to be one of the following

1 Teratoma or dermoid cyst
2 Neurogenic tumour (neuro fibroma or ganglio neuroma)
3 Tumour of thyroid tissue
4 Tumour of thymic origin
5 Lipoma
6 Cystic hygroma

Any one of these tumours may be very large and cause breathlessness due to reduction in lung volume (see Fig 169) or symptoms may arise from local pressure on some structure such as a bronchus or vein In these circumstances the tumour should be removed unless there is some reason such as senility or respiratory insufficiency for believing that the risks of operation are unjustifiable To quote an example in which surgical treatment was considered to involve too great a hazard a parson aged 67 who had suffered from progressive breathlessness for many years and latterly from recurrent broncho pneumonia was shown to have a very large mediastinal tumour (see Fig 169) and secondary bronchiectasis As he was very frail the risks of an attempt to remove the mass seemed even greater than those of continuing with the tumour *in situ* However as a tentative diagnosis of dermoid cyst had been made it was thought that it might be possible to reduce the size of the tumour

by aspiration, but this was not successful as the needle, which was of very large bore, was repeatedly blocked by locks of hair

Certain complications which are limited to a specific type of mediastinal tumour, e g infection of a dermoid cyst, thyrotoxic changes accompanying a



FIG 169 Oblique view of the chest of a man aged 67 with a massive dermoid cyst (This patient is older than any recorded case of dermoid cyst)

thyroid swelling or myasthenia gravis associated with a thymic tumour, make obvious the need for surgical removal of the mediastinal mass following proper medical preparation

The most common problem, however, is to decide what advice should be given to a patient shown to have a tumour of the mediastinum which is either causing no symptoms at all, for example, those discovered on mass radiography, or productive of minimal disturbance such as a mild ache in the chest If the tumour is left *in situ* the prognosis is difficult to forecast as the pathological nature of the tumour is usually not known with certainty and if it

were, the outlook would remain doubtful as the natural history of any given type of neoplasm is uncertain

Many reasons for advocating operative removal in all cases of mediastinal tumour have been advanced, but it is not always possible to find factual or statistical evidence to support such a policy For example, it is often said that all these tumours will gradually increase in size and sooner or later cause symptoms, but this is not true for although some cases show steady progressive enlargement, others remain unaltered in size over a period of many years and it is impossible to forecast which event is the most likely

Likewise the incidence of complications is not known with certainty although the evidence is gradually accumulating Rusby (1944) states that malignant change was present in 12 9 per cent of 209 published cases of teratomata and dermoid cysts Kent and others (1944) studied the reports of 74 cases of mediastinal neurogenic tumour in the literature and found that 20 3 per cent were stated to show malignant change but as the cases included children with neuroblastomata and as malignancy is sometimes diagnosed simply on the finding of marked cellularity of the tumour it would not be fair to assume that there is a one in five chance of a s litary neurogenic tumour of the mediastinum being malignant for this would undoubtedly exaggerate the malignant potentialities of such a tumour In the case of thyroid tumours the incidence of malignant change thyrotoxi :osis, and haemorrhage into a cyst appears to be the same as for goitres n the neck

From the available evidence it would seem right to recommend a patient harbouring a symptomless mediastinal tumour to have it removed provided the general health is satisfactory

On the other hand, I believe it is quite justifiable to keep under intermittent radiological observation those patients who have extraneous disabilities which would increase the hazards of operation, and those over the age of 60 chest films being taken every three months for the first year after discovery twice in the second year, and subsequently annually Any increase in the size of the mediastinal opacity would be an indication to reconsider the advisability of operation

As thymic neoplasms are particularly liable to show malignant characteristics and are frequently associated with myasthenia gravis, there are especially good reasons for advocating active treatment It is therefore inadvisable to dvocate a policy of observation when there is reason to suspect that a tumour has origin in the thymus

Pre-operative Preparation

The investigation of a patient thought to possess a mediastinal tumour has

been discussed in previous chapters but it may be helpful to emphasize certain points of importance to the surgeon In addition to a detailed clinical and radiological examination it is frequently advisable to examine the bronchial tree by bronchoscopy so that compression of the trachea or of a large bronchus may not pass unrecognized this examination may also be of value in confirming that the tumour is truly of mediastinal origin and not secondary to a lesion of the bronchial tree

If, after these investigations, there is still doubt as to whether the tumour is in the lung or whether it is in the mediastinum, an artificial pneumothorax should be induced if possible and the patient re examined radiologically as it is then often possible to demonstrate that the lung has collapsed away from a mediastinal tumour or, conversely, that an intrapulmonary tumour has collapsed down with the lung If operation is contemplated regardless of whether the tumour be intrapulmonary or mediastinal, the distinction between the two becomes of less importance, although a correct answer may influence the surgeon considerably in selecting his method of operative exposure for example, a tumour of thymic origin might be explored by splitting the sternum, which would be a useless exposure for a tumour in the pectoral segment of an upper lobe, and yet it is possible that each might throw a very similar radiological shadow

Inspection of a tumour by thoracoscopy after inducing a pneumothorax may be interesting, but is rarely called for as it is extremely unlikely that any information of practical value will be obtained by this means, it is, for example, almost invariably impossible to determine the pathological nature of a tumour by inspection of its surface

Breathing exercises should be practised during the week before operation Occasionally there are septic complications such as purulent bronchitis or suppuration in a dermoid cyst and these should be controlled as far as possible by suitable chemotherapy, combining this with postural drainage if the latter can be employed to aid expectoration of secretions

Complications of certain specific types of tumour such as thyrotoxicosis and myasthenia gravis obviously require medical treatment so as to bring the general systemic effects under control

Anaesthesia and intravenous therapy during operation follow the general principles described for the removal of broncho-pulmonary neoplasms

Operative Procedure

A transpleural exposure through a wide postero lateral thoracotomy incision will allow the removal of almost any type of mediastinal neoplasm and is therefore generally employed The level at which the chest is entered depends upon the site of the tumour If the tumour is in the *anterior media-*

stinum, the fourth rib bed or intercostal space is suitable for those in the superior part, the fifth rib for those centrally placed, and the sixth rib for those in the inferior part When the growth is sited posteriorly, the exploration should be made through the intercostal space or rib-bed, the posterior end of which overlies the centre of the tumour this generalization is not applicable to tumours in the superior part of the chest as the exposure is obstructed by the shoulder-girdle if a postero-lateral thoracotomy is attempted above the level of the fourth rib, which should therefore be regarded as the uppermost limit for entering the chest by this approach

British thoracic surgeons are sometimes criticized for their addiction to the postero-lateral approach, but this addiction is the result of frequent dis-appointments with other means of entering the chest The postero-lateral incision gives almost unlimited exposure as it may be enlarged by division of the posterior ends of as many ribs and intercostal bundles above and below as required This mode of access has an additional advantage in the case of large anteriorly placed tumours for it allows the surgeon when freeing the growth to see and protect the great vessels which lie behind the growth, and this is a great comfort denied to the operator working through a median sternotomy or even an antero-lateral thoracotomy

Postero-lateral incisions, however, do not permit extending the operation into the neck, a disadvantage which is only of significance in the case of certain thyroid and thymic tumours, for these may obtain their blood-supply from the vessels in the neck On the whole, if a diagnosis of thymic tumour has been made, it is probably best to undertake its removal by an extra-pleural operation after splitting the sternum in the mid line (median sterno-tomy) The whole length of the sternum may be divided, or the section ma[y] be carried from the suprasternal notch down to the level of the third or fo[urth] intercostal space, at which level the sternum is also divided transversely

In the case of thyroid tumours having an attachment to the thyroid gl[and] in the neck, removal is often possible through the 'collar' incision routin[ely] employed for operations on cervical goitre after division of the superior a[nd] middle thyroid vessels and separation of the lateral lobe from its deeper part and from the isthmus, gentle traction will often allow the mediastinal part to be drawn up into the neck, so exposing its blood supply from the inferior thyroid vessels If the mediastinal part is too large to be drawn through the thoracic inlet into the neck and the tumour is partially cystic, a finger may be used to break up the cystic part so that the contents can be evacuated and subsequently it may be possible to draw the capsular part into the neck If the operator does not approve of this rather messy manœuvre or if the tumour is not cystic, the cervical incision must be combined with median section of the upper part of the sternum For thyroid tumours situated low down in the

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mediastinum and for those lying posteriorly a postero lateral thoracotomy is almost certainly the best approach

The separation of tumours from their surroundings follows general surgical principles but there are a few points referable to specific types of tumour which are worth mentioning

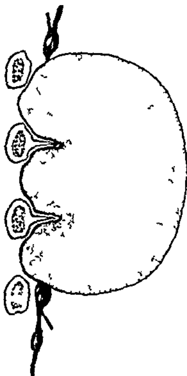


Fig 170 Diagram representing a sagittal section through a neurogenic tumour and adjacent ribs to show the dovetailing between tumour tissue and ribs

Teratomata and dermoid cysts are often densely adherent to some of the neighbouring tissues particularly to the pericardium and the operator must expect a difficult dissection which may require much patience As the mediastinal pleura of both sides may be firmly attached to the tumour it is sometimes impossible to avoid opening the pleural cavity of the side opposite to that of the thoracotomy so the anaesthetist must be fully prepared to carry on under these conditions In the case of large dermoid cysts the operation may be made easier if after opening the chest the size of the tumour is reduced by making a small opening into the cyst and aspirating the contents with a sucker Infected dermoid cysts are likely to be most densely adherent and to have a greater blood supply than those without infection in many such cases it is safer to perform a preliminary drainage operation and subsequently to excise the residual sac particularly if a secondary communication with the bronchial tree has developed

A neurogenic tumour is usually a sessile tumour lying in the paravertebral gutter in the course of the sympathetic chain which may be seen to enter the upper and lower extremities of the mass Although many of these tumours shell out very easily others are not so easily removed as they may form lobules protruding into the intercostal spaces and the ribs may form sharp ridges of new bone projecting into the neoplasm so that the mass is fixed to the chest wall in dovetail fashion (see Fig 170)

In difficult cases after narrowing the site of attachment to the area of dense adherence it is usually easiest to complete the removal by forcing the plane of separation with the fingers as rapidly as possible and then placing a large gauze swab over the raw area to control the bleeding the bleeding points are subsequently picked up individually and controlled with ligatures

This method appears crude but it is preferable to a painstaking dissection for the latter may be almost impossible owing to the rigidity of the tumour preventing the surgeon having access to the vessels which enter the tumour from the chest wall

In the case of dumb bell tumours which have been recognized as such by the presence of pressure effects on the cord there can be no doubt that removal of the intraspinal portion by laminectomy should take precedence of excision of the intrathoracic portion It might be argued that a transpleural operation would permit withdrawal of the intraspinal projection through the enlarged intervertebral foramen but this is almost certain to be impossible if the intra spinal portion is large enough to give rise to pressure effects

In all cases of transpleural removal of mediastinal neoplasms it is wise to drain the pleural cavity with a water seal drain for at least 48 hours after operation

Results of Surgical Treatment

It is quite impossible to obtain a fair impression of the results of operation from the literature as successful cases are much more likely to be published than failures thus belittling the hazards of operation and conversely most reviews of the subject include cases treated many years ago when the risks associated with thoracic surgery were infinitely higher than they are today With the above facts in mind it is interesting to note that Rusby (1944) found reports of 60 patients in whom excision of a teratoma or dermoid cyst had been attempted in 53 the tumour was completely removed and the patient cured in 4 others improvement was obtained but a persistent sinus followed operation and there were 3 deaths Rusby also found that 14 out of 31 cases treated simply by drainage of the cyst died but this appalling mortality is explained by the facts that many of these reports were found in the earlier publications and that most of the patients treated in this way during recent years were gravely ill with infected cysts

Kent and others report a 15 per cent operative mortality for the removal of intrathoracic neurogenic tumours but again this high death rate is accounted for by the inclusion of the earlier case reports

The death rate of excision of innocent mediastinal tumours at the present time probably does not exceed 5 per cent If successfully removed the patient should be restored to full health

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INDEX OF AUTHORS

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